(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
24 June 2004 (24.06.2004)

PCT

(10) International Publication Number
WO 2004/053079 A2

(51) International Patent Classification[7]: C12N

(21) International Application Number: PCT/US2003/038855

(22) International Filing Date: 8 December 2003 (08.12.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/431,321	6 December 2002 (06.12.2002)	US
60/431,301	6 December 2002 (06.12.2002)	US
60/484,584	30 June 2003 (30.06.2003)	US
60/518,607	7 November 2003 (07.11.2003)	US

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(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2004/053079 A2

(54) Title: COMPOSITIONS, SPLICE VARIANTS AND METHODS RELATING TO OVARIAN SPECIFIC GENES AND PROTEINS

(57) Abstract: The present invention relates to newly identified nucleic acid molecules and polypeptides present in normal and neoplastic ovarian cells, including fragments, variants and derivatives of the nucleic acids and polypeptides. The present invention also relates to antibodies to the polypeptides of the invention, as well as agonists and antagonists of the polypeptides of the invention. The invention also relates to compositions containing the nucleic acid molecules, polypeptides, antibodies, agonists and antagonists of the invention and methods for the use of these compositions. These uses include identifying, diagnosing, monitoring, staging, imaging and treating ovarian cancer and non-cancerous disease states in ovarian, identifying ovarian tissue, monitoring and identifying and/or designing agonists and antagonists of polypeptides of the invention. The uses also include gene therapy, production of transgenic animals and cells, and production of engineered ovarian tissue for treatment and research.

COMPOSITIONS, SPLICE VARIANTS AND METHODS RELATING TO OVARIAN SPECIFIC GENES AND PROTEINS

INTRODUCTION

This application claims the benefit of priority from U.S. Provisional Patent Application Serial No. 60/431,321 filed December 6, 2002, U.S. Provisional Patent Application Serial No. 60/431,301 filed December 6, 2002, U.S. Provisional Patent Application Serial No. 60/484,584 filed June 30, 2003 and U.S. Provisional Patent Application Serial No. 60/518,607, filed November 7, 2003 which are herein incorporated by reference in their entireties.

FIELD OF THE INVENTION

The present invention relates to newly identified nucleic acids and polypeptides present in normal and neoplastic ovarian cells, including fragments, variants and derivatives of the nucleic acids and polypeptides. The present invention also relates to antibodies to the polypeptides of the invention, as well as agonists and antagonists of the polypeptides of the invention. The invention also relates to compositions comprising the nucleic acids, polypeptides, antibodies, post translational modifications (PTMs), variants, derivatives, agonists and antagonists thereto and methods for the use of these compositions. These uses include identifying, diagnosing, monitoring, staging, imaging and treating ovarian cancer and/or non-cancerous disease states in ovarian, identifying ovarian tissue and monitoring and identifying and/or designing agonists and antagonists of polypeptides of the invention. The uses also include gene therapy, therapeutic molecules including but not limited to antibodies or antisense molecules, production of transgenic animals and cells, and production of engineered ovarian tissue for treatment and research.

BACKGROUND OF THE INVENTION

Cancer of the ovaries is the fourth-most common cause of cancer death in women in the United States, with more than 23,000 new cases and roughly 14,000 deaths predicted for the year 2001. Shridhar, V. *et al., Cancer Res.* 61(15):5895-904 (2001); Memarzadeh, S. & Berek, J. S., *J. Reprod. Med.* 46(7):621-29 (2001). The incidence of ovarian cancer is of serious concern worldwide, with an estimated 191,000 new cases predicted annually. Runnebaum, I. B. & Stickeler, E., *J. Cancer Res. Clin. Oncol.* 127(2):73-79 (2001). These numbers continue to rise today. In the United States

alone, it is estimated there will be 25,400 new cases of ovarian cancer, and 14,300 deaths due to ovarian cancer in 2003. (American Cancer Society Website: cancer.org on the world wide web). Unfortunately, women with ovarian cancer are typically asymptomatic until the disease has metastasized. Because effective screening for ovarian cancer is not available, roughly 70% of women diagnosed have an advanced stage of the cancer with a five-year survival rate of ~25-30%. Memarzadeh, S. & Berek, J. S., *supra*; Nunns, D. *et al., Obstet. Gynecol. Surv.* 55(12):746-51. Conversely, women diagnosed with early stage ovarian cancer enjoy considerably higher survival rates. Werness, B. A. & Eltabbakh, G. H., *Int'l. J. Gynecol. Pathol.* 20(1):48-63 (2001). Although our understanding of the etiology of ovarian cancer is incomplete, the results of extensive research in this area point to a combination of age, genetics, reproductive, and dietary/environmental factors. Age is a key risk factor in the development of ovarian cancer: while the risk for developing ovarian cancer before the age of 30 is slim, the incidence of ovarian cancer rises linearly between ages 30 to 50, increasing at a slower rate thereafter, with the highest incidence being among septagenarian women. Jeanne M. Schilder *et al.*, *Hereditary Ovarian Cancer: Clinical Syndromes and Management*, in Ovarian Cancer 182 (Stephen C. Rubin & Gregory P. Sutton eds., 2d ed. 2001).

With respect to genetic factors, a family history of ovarian cancer is the most significant risk factor in the development of the disease, with that risk depending on the number of affected family members, the degree of their relationship to the woman, and which particular first degree relatives are affected by the disease. Id. Mutations in several genes have been associated with ovarian cancer, including BRCA1 and BRCA2, both of which play a key role in the development of breast cancer, as well as hMSH2 and hMLH1, both of which are associated with hereditary non-polyposis colon cancer. Katherine Y. Look, *Epidemiology, Etiology, and Screening of Ovarian Cancer*, in Ovarian Cancer 169, 171-73 (Stephen C. Rubin & Gregory P. Sutton eds., 2d ed. 2001). BRCA1, located on chromosome 17, and BRCA2, located on chromosome 13, are tumor suppressor genes implicated in DNA repair; mutations in these genes are linked to roughly 10% of ovarian cancers. *Id.* at 171-72; Schilder *et al., supra* at 185-86. hMSH2 and hMLH1 are associated with DNA mismatch repair, and are located on chromosomes 2 and 3, respectively; it has been reported that roughly 3% of hereditary ovarian carcinomas are due to mutations in these genes. Look, *supra* at 173; Schilder *et al., supra* at 184, 188-89.

Reproductive factors have also been associated with an increased or reduced risk of ovarian cancer. Late menopause, nulliparity, and early age at menarche have all been linked with an elevated risk of ovarian cancer. Schilder *et al., supra* at 182. One theory hypothesizes that these factors increase the number of ovulatory cycles over the course of a woman's life, leading to "incessant ovulation," which is thought to be the primary cause of mutations to the ovarian epithelium. *Id*; Laura J. Havrilesky & Andrew Berchuck, *Molecular Alterations in Sporadic Ovarian Cancer*, in Ovarian Cancer 25 (Stephen C. Rubin & Gregory P. Sutton eds., 2d ed. 2001). The mutations may be explained by the fact that ovulation results in the destruction and repair of that epithelium, necessitating increased cell division, thereby increasing the possibility that an undetected mutation will occur. *Id.* Support for this theory may be found in the fact that pregnancy, lactation, and the use of oral contraceptives, all of which suppress ovulation, confer a protective effect with respect to developing ovarian cancer. *Id.*

Among dietary/environmental factors, there would appear to be an association between high intake of animal fat or red meat and ovarian cancer, while the antioxidant Vitamin A, which prevents free radical formation and also assists in maintaining normal cellular differentiation, may offer a protective effect. Look, *supra* at 169. Reports have also associated asbestos and hydrous magnesium trisilicate (talc), the latter of which may be present in diaphragms and sanitary napkins. *Id.* at 169-70.

Current screening procedures for ovarian cancer, while of some utility, are quite limited in their diagnostic ability, a problem that is particularly acute at early stages of cancer progression when the disease is typically asymptomatic yet is most readily treatable. Walter J. Burdette, Cancer: Etiology, Diagnosis, and Treatment 166 (1998); Memarzadeh & Berek, *supra*; Runnebaum & Stickeler, *supra*; Werness & Eltabbakh, *supra*. Commonly used screening tests include biannual rectovaginal pelvic examination, radioimmunoassay to detect the CA-125 serum tumor marker, and transvaginal ultrasonography. Burdette, *supra* at 166.

Pelvic examination has failed to yield adequate numbers of early diagnoses, and the other methods are not sufficiently accurate. *Id.* One study reported that only 15% of patients who suffered from ovarian cancer were diagnosed with the disease at the time of their pelvic examination. Look, *supra* at 174. Moreover, the CA-125 test is prone to giving false positives in pre-menopausal women and has been reported to be of low predictive value in post-menopausal women. *Id.* at 174-75. Although transvaginal

ultrasonography is now the preferred procedure for screening for ovarian cancer, it is unable to distinguish reliably between benign and malignant tumors, and also cannot locate primary peritoneal malignancies or ovarian cancer if the ovary size is normal. Schilder *et al., supra* at 194-95. While genetic testing for mutations of the BRCA1, BRCA2, hMSH2, and hMLH1 genes is now available, these tests may be too costly for some patients and may also yield false negative or indeterminate results. Schilder *et al., supra* at 191-94.

The staging of ovarian cancer, which is accomplished through surgical exploration, is crucial in determining the course of treatment and management of the disease. AJCC Cancer Staging Handbook 187 (Irvin D. Fleming *et al.* eds., 5th ed. 1998); Burdette, *supra* at 170; Memarzadeh & Berek, *supra*; Shridhar *et al., supra*. Staging is performed by reference to the classification system developed by the International Federation of Gynecology and Obstetrics. David H. Moore, *Primary Surgical Management of Early Epithelial Ovarian Carcinoma*, in Ovarian Cancer 203 (Stephen C. Rubin & Gregory P. Sutton eds., 2d ed. 2001); Fleming *et al.* eds., *supra* at 188. Stage I ovarian cancer is characterized by tumor growth that is limited to the ovaries and is comprised of three substages. *Id.* In substage IA, tumor growth is limited to one ovary, there is no tumor on the external surface of the ovary, the ovarian capsule is intact, and no malignant cells are present in ascites or peritoneal washings. *Id.* Substage IB is identical to A1, except that tumor growth is limited to both ovaries. *Id.* Substage IC refers to the presence of tumor growth limited to one or both ovaries, and also includes one or more of the following characteristics: capsule rupture, tumor growth on the surface of one or both ovaries, and malignant cells present in ascites or peritoneal washings. *Id.*

Stage II ovarian cancer refers to tumor growth involving one or both ovaries, along with pelvic extension. *Id.* Substage IIA involves extension and/or implants on the uterus and/or fallopian tubes, with no malignant cells in the ascites or peritoneal washings, while substage IIB involves extension into other pelvic organs and tissues, again with no malignant cells in the ascites or peritoneal washings. *Id.* Substage IIC involves pelvic extension as in IIA or IIB, but with malignant cells in the ascites or peritoneal washings. *Id.*

Stage III ovarian cancer involves tumor growth in one or both ovaries, with peritoneal metastasis beyond the pelvis confirmed by microscope and/or metastasis in the regional lymph nodes. *Id.* Substage IIIA is characterized by microscopic peritoneal

metastasis outside the pelvis, with substage IIIB involving macroscopic peritoneal metastasis outside the pelvis 2 cm or less in greatest dimension. *Id.* Substage IIIC is identical to IIIB, except that the metastasis is greater than 2 cm in greatest dimension and may include regional lymph node metastasis. *Id.* Lastly, Stage IV refers to the presence distant metastasis, excluding peritoneal metastasis. *Id.*

While surgical staging is currently the benchmark for assessing the management and treatment of ovarian cancer, it suffers from considerable drawbacks, including the invasiveness of the procedure, the potential for complications, as well as the potential for inaccuracy. Moore, *supra* at 206-208, 213. In view of these limitations, attention has turned to developing alternative staging methodologies through understanding differential gene expression in various stages of ovarian cancer and by obtaining various biomarkers to help better assess the progression of the disease. Vartiainen, J. *et al., Int'l J. Cancer*, 95(5):313-16 (2001); Shridhar *et al. supra*; Baekelandt, M. *et al., J. Clin. Oncol.* 18(22):3775-81.

The treatment of ovarian cancer typically involves a multiprong attack, with surgical intervention serving as the foundation of treatment. Dennis S. Chi & William J. Hoskins, *Primary Surgical Management of Advanced Epithelial Ovarian Cancer,* in Ovarian Cancer 241 (Stephen C. Rubin & Gregory P. Sutton eds., 2d ed. 2001). For example, in the case of epithelial ovarian cancer, which accounts for ~90% of cases of ovarian cancer, treatment typically consists of: (1) cytoreductive surgery, including total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and lymphadenectomy, followed by (2) adjuvant chemotherapy with paclitaxel and either cisplatin or carboplatin. Eltabbakh, G.H. & Awtrey, C.S., *Expert Op. Pharmacother.* 2(10):109-24. Despite a clinical response rate of 80% to the adjuvant therapy, most patients experience tumor recurrence within three years of treatment. *Id.* Certain patients may undergo a second cytoreductive surgery and/or second-line chemotherapy. Memarzadeh & Berek, *supra*.

From the foregoing, it is clear that procedures used for detecting, diagnosing, monitoring, staging, prognosticating, and preventing the recurrence of ovarian cancer are of critical importance to the outcome of the patient. Moreover, current procedures, while helpful in each of these analyses, are limited by their specificity, sensitivity, invasiveness, and/or their cost. As such, highly specific and sensitive procedures that would operate by

way of detecting novel markers in cells, tissues, or bodily fluids, with minimal invasiveness and at a reasonable cost, would be highly desirable.

Breast cancer, also referred to as mammary tumor cancer, is the second most common cancer among women, accounting for a third of the cancers diagnosed in the United States. One in nine women will develop breast cancer in her lifetime and about 192,000 new cases of breast cancer are diagnosed annually with about 42,000 deaths. Bevers, *Primary Prevention of Breast Cancer*, in Breast Cancer, 20-54 (Kelly K Hunt et al., ed., 2001); Kochanek *et al.*, 49 *Nat'l. Vital Statistics Reports* 1, 14 (2001). Breast cancer is extremely rare in women younger than 20 and is very rare in women under 30. The incidence of breast cancer rises with age and becomes significant by age 50. White Non-Hispanic women have the highest incidence rate for breast cancer and Korean women have the lowest. Increased prevalence of the genetic mutations BRCA1 and BRCA2 that promote breast and other cancers are found in Ashkenazi Jews. African American women have the highest mortality rate for breast cancer among these same groups (31 per 100,000), while Chinese women have the lowest at 11 per 100,000. Although men can get breast cancer, this is extremely rare. In the United States it is estimated there will be 212,600 new cases of breast cancer and 40,200 deaths due to breast cancer in 2003. (American Cancer Society Website: cancer.org on the world wide web). With the exception of those cases with associated genetic factors, precise causes of breast cancer are not known.

In the treatment of breast cancer, there is considerable emphasis on detection and risk assessment because early and accurate staging of breast cancer has a significant impact on survival. For example, breast cancer detected at an early stage (stage T0, discussed below) has a five-year survival rate of 92%. Conversely, if the cancer is not detected until a late stage (i.e., stage T4 (IV)), the five-year survival rate is reduced to 13%. AJCC Cancer Staging Handbook pp. 164-65 (Irvin D. Fleming *et al.* eds., 5th ed. 1998). Some detection techniques, such as mammography and biopsy, involve increased discomfort, expense, and/or radiation, and are only prescribed only to patients with an increased risk of breast cancer.

Current methods for predicting or detecting breast cancer risk are not optimal. One method for predicting the relative risk of breast cancer is by examining a patient's risk factors and pursuing aggressive diagnostic and treatment regiments for high risk patients. A patient's risk of breast cancer has been positively associated with increasing age,

nulliparity, family history of breast cancer, personal history of breast cancer, early menarche, late menopause, late age of first full term pregnancy, prior proliferative breast disease, irradiation of the breast at an early age and a personal history of malignancy. Lifestyle factors such as fat consumption, alcohol consumption, education, and socioeconomic status have also been associated with an increased incidence of breast cancer although a direct cause and effect relationship has not been established. While these risk factors are statistically significant, their weak association with breast cancer limited their usefulness. Most women who develop breast cancer have none of the risk factors listed above, other than the risk that comes with growing older. NIH Publication No. 00-1556 (2000).

Current screening methods for detecting cancer, such as breast self exam, ultrasound, and mammography have drawbacks that reduce their effectiveness or prevent their widespread adoption. Breast self exams, while useful, are unreliable for the detection of breast cancer in the initial stages where the tumor is small and difficult to detect by palpation. Ultrasound measurements require skilled operators at an increased expense. Mammography, while sensitive, is subject to over diagnosis in the detection of lesions that have questionable malignant potential. There is also the fear of the radiation used in mammography because prior chest radiation is a factor associated with an increase incidence of breast cancer.

At this time, there are no adequate methods of breast cancer prevention. The current methods of breast cancer prevention involve prophylactic mastectomy (mastectomy performed before cancer diagnosis) and chemoprevention (chemotherapy before cancer diagnosis) which are drastic measures that limit their adoption even among women with increased risk of breast cancer. Bevers, *supra*.

A number of genetic markers have been associated with breast cancer. Examples of these markers include carcinoembryonic antigen (CEA) (Mughal *et al., JAMA* 249:1881 (1983)), MUC-1 (Frische and Liu, *J. Clin. Ligand* 22:320 (2000)), HER-2/neu (Haris *et al., Proc.Am.Soc.Clin.Oncology* 15:A96 (1996)), uPA, PAI-1, LPA, LPC, RAK and BRCA (Esteva and Fritsche, *Serum and Tissue Markers for Breast Cancer*, in <u>Breast Cancer</u>, 286-308 (2001)). These markers have problems with limited sensitivity, low correlation, and false negatives which limit their use for initial diagnosis. For example, while the BRCA1 gene mutation is useful as an indicator of an increased risk for breast cancer, it has limited use in cancer diagnosis because only 6.2 % of breast cancers are

BRCA1 positive. Malone *et al., JAMA* 279:922 (1998). See also, Mewman *et al., JAMA* 279:915 (1998) (correlation of only 3.3%).

There are four primary classifications of breast cancer varying by the site of origin and the extent of disease development.

I. Ductal carcinoma in situ (DCIS): Malignant transformation of ductal epithelial cells that remain in their normal position. DCIS is a purely localized disease, incapable of metastasis.

II. Invasive ductal carcinoma (IDC): Malignancy of the ductal epithelial cells breaking through the basal membrane and into the supporting tissue of the breast. IDC may eventually spread elsewhere in the body.

III. Lobular carcinoma in situ (LCIS): Malignancy arising in a single lobule of the breast that fail to extend through the lobule wall, it generally remains localized.

IV. Infiltrating lobular carcinoma (ILC): Malignancy arising in a single lobule of the breast and invading directly through the lobule wall into adjacent tissues. By virtue of its invasion beyond the lobule wall, ILC may penetrate lymphatics and blood vessels and spread to distant sites.

For purpose of determining prognosis and treatment, these four breast cancer types have been staged according to the size of the primary tumor (T), the involvement of lymph nodes (N), and the presence of metastasis (M). Although DCIS by definition represents localized stage I disease, the other forms of breast cancer may range from stage II to stage IV. There are additional prognostic factors that further serve to guide surgical and medical intervention. The most common ones are total number of lymph nodes involved, ER (estrogen receptor) status, Her2/neu receptor status and histologic grades.

Breast cancers are diagnosed into the appropriate stage categories recognizing that different treatments are more effective for different stages of cancer. Stage TX indicates that primary tumor cannot be assessed (i.e., tumor was removed or breast tissue was removed). Stage T0 is characterized by abnormalities such as hyperplasia but with no evidence of primary tumor. Stage Tis is characterized by carcinoma in situ, intraductal carcinoma, lobular carcinoma in situ, or Paget's disease of the nipple with no tumor. Stage T1 (I) is characterized as having a tumor of 2 cm or less in the greatest dimension. Within stage T1, Tmic indicates microinvasion of 0.1 cm or less, T1a indicates a tumor of between 0.1 to 0.5 cm, T1b indicates a tumor of between 0.5 to 1 cm, and T1c indicates tumors of between 1 cm to 2 cm. Stage T2 (II) is characterized by tumors from 2 cm to 5

cm in the greatest dimension. Tumors greater than 5 cm in size are classified as stage T3 (III). Stage T4 (IV) indicates a tumor of any size with extension to the chest wall or skin. Within stage T4, T4a indicates extension of the tumor to the chest wall, T4b indicates edema or ulceration of the skin of the breast or satellite skin nodules confined to the same breast, T4c indicates a combination of T4a and T4b, and T4d indicates inflammatory carcinoma. AJCC Cancer Staging Handbook pp. 159-70 (Irvin D. Fleming *et al.* eds., 5th ed. 1998). In addition to standard staging, breast tumors may be classified according to their estrogen receptor and progesterone receptor protein status. Fisher *et al., Breast Cancer Research and Treatment* 7:147 (1986). Additional pathological status, such as HER2/neu status may also be useful. Thor *et al., J.Nat'l.Cancer Inst.* 90:1346 (1998); Paik *et al., J.Nat'l.Cancer Inst.* 90:1361 (1998); Hutchins *et al., Proc. Am. Soc. Clin. Oncology* 17:A2 (1998).; and Simpson *et al., J.Clin.Oncology* 18:2059 (2000).

In addition to the staging of the primary tumor, breast cancer metastases to regional lymph nodes may be staged. Stage NX indicates that the lymph nodes cannot be assessed (e.g., previously removed). Stage N0 indicates no regional lymph node metastasis. Stage N1 indicates metastasis to movable ipsilateral axillary lymph nodes. Stage N2 indicates metastasis to ipsilateral axillary lymph nodes fixed to one another or to other structures. Stage N3 indicates metastasis to ipsilateral internal mammary lymph nodes. *Id.*

Stage determination has potential prognostic value and provides criteria for designing optimal therapy. Simpson *et al., J. Clin. Oncology* 18:2059 (2000). Generally, pathological staging of breast cancer is preferable to clinical staging because the former gives a more accurate prognosis. However, clinical staging would be preferred if it were as accurate as pathological staging because it does not depend on an invasive procedure to obtain tissue for pathological evaluation. Staging of breast cancer would be improved by detecting new markers in cells, tissues, or bodily fluids which could differentiate between different stages of invasion. Progress in this field will allow more rapid and reliable method for treating breast cancer patients.

Treatment of breast cancer is generally decided after an accurate staging of the primary tumor. Primary treatment options include breast conserving therapy (lumpectomy, breast irradiation, and surgical staging of the axilla), and modified radical mastectomy. Additional treatments include chemotherapy, regional irradiation, and, in extreme cases, terminating estrogen production by ovarian ablation.

Until recently, the customary treatment for all breast cancer was mastectomy. Fonseca *et al., Annals of Internal Medicine* 127:1013 (1997). However, recent data indicate that less radical procedures may be equally effective, in terms of survival, for early stage breast cancer. Fisher *et al., J. of Clinical Oncology* 16:441 (1998). The treatment options for a patient with early stage breast cancer (i.e., stage Tis) may be breast-sparing surgery followed by localized radiation therapy at the breast. Alternatively, mastectomy optionally coupled with radiation or breast reconstruction may be employed. These treatment methods are equally effective in the early stages of breast cancer.

Patients with stage I and stage II breast cancer require surgery with chemotherapy and/or hormonal therapy. Surgery is of limited use in stage III and stage IV patients. Thus, these patients are better candidates for chemotherapy and radiation therapy with surgery limited to biopsy to permit initial staging or subsequent restaging because cancer is rarely curative at this stage of the disease. <u>AJCC Cancer Staging Handbook</u> 84, 164-65 (Irvin D. Fleming *et al.* eds., 5^{th} ed.1998).

In an effort to provide more treatment options to patients, efforts are underway to define an earlier stage of breast cancer with low recurrence which could be treated with lumpectomy without postoperative radiation treatment. While a number of attempts have been made to classify early stage breast cancer, no consensus recommendation on postoperative radiation treatment has been obtained from these studies. Page *et al., Cancer* 75:1219 (1995); Fisher *et al., Cancer* 75:1223 (1995); Silverstein *et al., Cancer* 77:2267 (1996).

As discussed above, each of the methods for diagnosing and staging ovarian, and breast cancer is limited by the technology employed. Accordingly, there is need for sensitive molecular and cellular markers for the detection of ovarian, and breast cancer as well as pancreatic cancer. There is a need for molecular markers for the accurate staging, including clinical and pathological staging, of ovarian, pancreatic or breast cancers to optimize treatment methods. Finally, there is a need for sensitive molecular and cellular markers to monitor the progress of cancer treatments, including markers that can detect recurrence of ovarian, pancreatic or breast cancers following remission.

The present invention provides alternative methods of treating ovarian, pancreatic or breast cancer that overcome the limitations of conventional therapeutic methods as well as offer additional advantages that will be apparent from the detailed description below.

Growth and metastasis of solid tumors are also dependent on angiogenesis. Folkman, J., 1986, *Cancer Research*, 46, 467-473; Folkman, J., 1989, *Journal of the National Cancer Institute*, 82, 4-6. It has been shown, for example, that tumors which enlarge to greater than 2 mm must obtain their own blood supply and do so by inducing the growth of new capillary blood vessels. Once these new blood vessels become embedded in the tumor, they provide a means for tumor cells to enter the circulation and metastasize to distant sites such as liver, lung or bone. Weidner, N., *et al.*, 1991, *The New England Journal of Medicine*, 324(1), 1-8.

Angiogenesis, defined as the growth or sprouting of new blood vessels from existing vessels, is a complex process that primarily occurs during embryonic development. The process is distinct from vasculogenesis, in that the new endothelial cells lining the vessel arise from proliferation of existing cells, rather than differentiating from stem cells. The process is invasive and dependent upon proteolyisis of the extracellular matrix (ECM), migration of new endothelial cells, and synthesis of new matrix components. Angiogenesis occurs during embryogenic development of the circulatory system; however, in adult humans, angiogenesis only occurs as a response to a pathological condition (except during the reproductive cycle in women).

Under normal physiological conditions in adults, angiogenesis takes place only in very restricted situations such as hair growth and wounding healing. Auerbach, W. and Auerbach, R., 1994, *Pharmacol Ther.* 63(3):265-3 11; Ribatti et al.,1991, *Haematologica* 76(4):3 11-20; Risau, 1997, *Nature* 386(6626):67 1-4. Angiogenesis progresses by a stimulus which results in the formation of a migrating column of endothelial cells. Proteolytic activity is focused at the advancing tip of this "vascular sprout", which breaks down the ECM sufficiently to permit the column of cells to infiltrate and migrate. Behind the advancing front, the endothelial cells differentiate and begin to adhere to each other, thus forming a new basement membrane. The cells then cease proliferation and finally define a lumen for the new arteriole or capillary.

Unregulated angiogenesis has gradually been recognized to be responsible for a wide range of disorders, including, but not limited to, cancer, cardiovascular disease, rheumatoid arthritis, psoriasis and diabetic retinopathy. Folkman, 1995, *Nat Med* 1(1):27-31; Isner, 1999, *Circulation* 99(13): 1653-5; Koch, 1998, *Arthritis Rheum* 41(6):951-62; Walsh, 1999, *Rheumatology* (Oxford) 38(2):103-12; Ware and Simons, 1997, *Nat Med* 3(2): 158-64.

Of particular interest is the observation that angiogenesis is required by solid tumors for their growth and metastases. Folkman, 1986 *supra*; Folkman 1990, *J Natl. Cancer Inst.*, 82(1) 4-6; Folkman, 1992, *Semin Cancer Biol* 3(2):65-71; Zetter, 1998, *Annu Rev Med* 49:407-24. A tumor usually begins as a single aberrant cell which can proliferate only to a size of a few cubic millimeters due to the distance from available capillary beds, and it can stay `dormant` without further growth and dissemination for a long period of time. Some tumor cells then switch to the angiogenic phenotype to activate endothelial cells, which proliferate and mature into new capillary blood vessels. These newly formed blood vessels not only allow for continued growth of the primary tumor, but also for the dissemination and recolonization of metastatic tumor cells. The precise mechanisms that control the angiogenic switch is not well understood, but it is believed that neovascularization of tumor mass results from the net balance of a multitude of angiogenesis stimulators and inhibitors Folkman, 1995, *supra*.

One of the most potent angiogenesis inhibitors is endostatin identified by O'Reilly and Folkman. O'Reilly et al., 1997, *Cell* 88(2):277-85; O'Reilly et al., 1994, *Cell* 79(2):3 15-28. Its discovery was based on the phenomenon that certain primary tumors can inhibit the growth of distant metastases. O'Reilly and Folkman hypothesized that a primary tumor initiates angiogenesis by generating angiogenic stimulators in excess of inhibitors. However, angiogenic inhibitors, by virtue of their longer half life in the circulation, reach the site of a secondary tumor in excess of the stimulators. The net result is the growth of primary tumor and inhibition of secondary tumor. Endostatin is one of a growing list of such angiogenesis inhibitors produced by primary tumors. It is a proteolytic fragment of a larger protein: endostatin is a 20 kDa fragment of collagen XVIII (amino acid H1132-K1315 in murine collagen XVIII). Endostatin has been shown to specifically inhibit endothelial cell proliferation in vitro and block angiogenesis in vivo. More importantly, administration of endostatin to tumor-bearing mice leads to significant tumor regression, and no toxicity or drug resistance has been observed even after multiple treatment cycles. Boehm et al., 1997, Nature 390(6658):404-407. The fact that endostatin targets genetically stable endothelial cells and inhibits a variety of solid tumors makes it a very attractive candidate for anticancer therapy. Fidler and Ellis, 1994, Cell 79(2):185-8; Gastl et al., 1997, Oncology 54(3):177-84; Hinsbergh et al., 1999, Ann Oncol 10 Suppl 4:60-3. In addition, angiogenesis inhibitors have been shown to be more effective when combined with radiation and chemotherapeutic agents. Klement, 2000, J. Clin Invest, 105(8) R15-

24. Browder, 2000, Cancer Res. 6-(7) 1878-86, Arap et al., 1998, Science 279(5349):377-80; Mauceri et al., 1998, Nature 394(6690):287-91.

SUMMARY OF THE INVENTION

The present invention solves many needs in the art by providing nucleic acid molecules, polypeptides and antibodies thereto, variants and derivatives of the nucleic acids and polypeptides, and agonists and antagonists thereto that may be used to identify, diagnose, monitor, stage, image and treat ovarian cancer and/or non-cancerous disease states in ovarian; identify and monitor ovarian tissue; and identify and design agonists and antagonists of polypeptides of the invention. The invention also provides gene therapy, methods for producing transgenic animals and cells, and methods for producing engineered ovarian tissue for treatment and research.

One aspect of the present invention relates to nucleic acid molecules that are specific to ovarian cells, ovarian tissue and/or the ovarian organ. These ovarian specific nucleic acids (OSNAs) may be a naturally occurring cDNA, genomic DNA, RNA, or a fragment of one of these nucleic acids, or may be a non-naturally occurring nucleic acid molecule. If the OSNA is genomic DNA, then the OSNA is an ovarian specific gene (OSG). If the OSNA is RNA, then it is an ovarian specific transcript encoded by an OSG. Due to alternative splicing and transcriptional modification one OSG may encode for multiple ovarian specific RNAs. In a preferred embodiment, the nucleic acid molecule encodes a polypeptide that is specific to ovarian. More preferred is a nucleic acid molecule that encodes a polypeptide comprising an amino acid sequence of SEQ ID NO: 129-295. In another preferred embodiment, the nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 1-128. For the OSNA sequences listed herein, DEX0455_001.nt.1 corresponds to SEQ ID NO: 1. For sequences with multiple splice variants, the parent sequence DEX0455_001.nt.1, will be followed by DEX0455_001.nt.2, etc. for each splice variant. The sequences off the corresponding peptides are listed as DEX0455_001.aa.1, etc. For the mapping of all of the nucleotides and peptides, see the table in the Example 1 section below.

This aspect of the present invention also relates to nucleic acid molecules that selectively hybridize or exhibit substantial sequence similarity to nucleic acid molecules encoding an Ovarian Specific Protein (OSP), or that selectively hybridize or exhibit

substantial sequence similarity to an OSNA. In one embodiment of the present invention the nucleic acid molecule comprises an allelic variant of a nucleic acid molecule encoding an OSP, or an allelic variant of an OSNA. In another embodiment, the nucleic acid molecule comprises a part of a nucleic acid sequence that encodes an OSP or a part of a nucleic acid sequence of an OSNA.

In addition, this aspect of the present invention relates to a nucleic acid molecule further comprising one or more expression control sequences controlling the transcription and/or translation of all or a part of an OSNA or the transcription and/or translation of a nucleic acid molecule that encodes all or a fragment of an OSP.

Another aspect of the present invention relates to vectors and/or host cells comprising a nucleic acid molecule of this invention. In a preferred embodiment, the nucleic acid molecule of the vector and/or host cell encodes all or a fragment of an OSP. In another preferred embodiment, the nucleic acid molecule of the vector and/or host cell comprises all or a part of an OSNA. Vectors and host cells of the present invention are useful in the recombinant production of polypeptides, particularly OSPs of the present invention.

Another aspect of the present invention relates to polypeptides encoded by a nucleic acid molecule of this invention. The polypeptide may comprise either a fragment or a full-length protein. In a preferred embodiment, the polypeptide is an OSP. However, this aspect of the present invention also relates to mutant proteins (muteins) of OSPs, fusion proteins of which a portion is an OSP, and proteins and polypeptides encoded by allelic variants of an OSNA as provided herein.

A further aspect of the present invention is a novel splice variant which encodes an amino acid sequence that provides a novel region to be targeted for the generation of reagents that can be used in the detection and/or treatment of cancer. The novel amino acid sequence may lead to a unique protein structure, protein subcellular localization, biochemical processing or function. This information can be used to directly or indirectly facilitate the generation of additional or novel therapeutics or diagnostics. The nucleotide sequence in this novel splice variant can be used as a nucleic acid probe for the diagnosis and/or treatment of cancer.

Another aspect of the present invention relates to antibodies and other binders that specifically bind to a polypeptide of the instant invention. Accordingly antibodies or binders of the present invention specifically bind to OSPs, muteins, fusion proteins, and/or

homologous proteins or polypeptides encoded by allelic variants of an OSNA as provided herein.

Another aspect of the present invention relates to agonists and antagonists of the nucleic acid molecules and polypeptides of this invention. The agonists and antagonists of the instant invention may be used to treat ovarian cancer and non-cancerous disease states in ovarian and to produce engineered ovarian tissue.

Another aspect of the present invention relates to methods for using the nucleic acid molecules to detect or amplify nucleic acid molecules that have similar or identical nucleic acid sequences compared to the nucleic acid molecules described herein. Such methods are useful in identifying, diagnosing, monitoring, staging, imaging and treating ovarian cancer and/or non-cancerous disease states in ovarian. Such methods are also useful in identifying and/or monitoring ovarian tissue. In addition, measurement of levels of one or more of the nucleic acid molecules of this invention may be useful as a diagnostic as part of a panel in combination with known other markers, particularly those described in the ovarian cancer background section above.

Another aspect of the present invention relates to use of the nucleic acid molecules of this invention in gene therapy, for producing transgenic animals and cells, and for producing engineered ovarian tissue for treatment and research.

Another aspect of the present invention relates to methods for detecting polypeptides of this invention, preferably using antibodies thereto. Such methods are useful to identify, diagnose, monitor, stage, image and treat ovarian cancer and non-cancerous disease states in ovarian. In addition, measurement of levels of one or more of the polypeptides of this invention may be useful to identify, diagnose, monitor, stage, and/or image ovarian cancer in combination with known other markers, particularly those described in the ovarian cancer background section above. The polypeptides of the present invention can also be used to identify and/or monitor ovarian tissue, and to produce engineered ovarian tissue.

Yet another aspect of the present invention relates to a computer readable means of storing the nucleic acid and amino acid sequences of the invention. The records of the computer readable means can be accessed for reading and displaying of sequences for comparison, alignment and ordering of the sequences of the invention to other sequences. In addition, the computer records regarding the nucleic acid and/or amino acid sequences

and/or measurements of their levels may be used alone or in combination with other markers to diagnose ovarian related diseases.

BRIEF DESCRIPTION OF THE FIGURES

FIGURE 1 is a nucleotide sequence alignment which shows regions of similarity and difference between DEX0455_049.nt.5 (SEQ ID NO:96; EpCAM) and DEX0455_049.nt.1 (SEQ ID NO:92; Ovr232);

FIGURE 2 is an amino acid sequence alignment which shows regions of similarity and difference between DEX0455_049.aa.5 (SEQ ID NO:255; EpCAM) and DEX0455_049.aa.1 (SEQ ID NO:251; Ovr232);

FIGURE 3 is a nucleotide sequence alignment which shows regions of similarity and difference between DEX0455_049.nt.5 (SEQ ID NO:96; EpCAM) and DEX0455_049.nt.2 (SEQ ID NO:93; Ovr232v1);

FIGURE 4 is an amino acid sequence alignment which shows regions of similarity and difference between DEX0455_049.aa.5 (SEQ ID NO:255; EpCAM) and DEX0455_049.aa.2 (SEQ ID NO:252; Ovr232v1);

FIGURE 5 is a nucleotide sequence alignment which shows regions of similarity and difference between DEX0455_049.nt.5 (SEQ ID NO:96; EpCAM) and DEX0455_049.nt.3 (SEQ ID NO:94; Ovr232v2);

FIGURE 6 is an amino acid sequence alignment which shows regions of similarity and difference between DEX0455_049.aa.5 (SEQ ID NO:255; EpCAM) and DEX0455_049.aa.3 (SEQ ID NO:253; Ovr232v2);

FIGURE 7 is a nucleotide sequence alignment which shows regions of similarity and difference between DEX0455_049.nt.5 (SEQ ID NO:96; EpCAM) and DEX0455_049.nt.4 (SEQ ID NO:95; Ovr232v3);

FIGURE 8 is an amino acid sequence alignment which shows regions of similarity and difference between DEX0455_049.aa.5 (SEQ ID NO:255; EpCAM) and DEX0455_049.aa.4 (SEQ ID NO:254; Ovr232v3);

FIGURE 9 is a nucleotide sequence alignment which shows regions of similarity and difference between DEX0455_051.nt.1 (SEQ ID NO:98; Ovr107) and DEX0455_051.nt.2 (SEQ ID NO:99);

FIGURE 10 is an amino acid sequence alignment which shows regions of similarity and difference between DEX0455_051.aa.1 (SEQ ID NO:258; Ovr107) and DEX0455_051.aa.3 (SEQ ID NO:260);

FIGURE 11 is an amino acid sequence alignment which shows regions of similarity and difference between DEX0455_051.aa.1 (SEQ ID NO:258; Ovr107) and DEX0455_051.aa.2 (SEQ ID NO:259);

FIGURE 12 is a nucleotide sequence alignment which shows regions of similarity and difference between DEX0455_051.nt.1 (SEQ ID NO:98; Ovr107) and DEX0455_051.nt.3 (SEQ ID NO:100);

FIGURE 13 is a nucleotide sequence alignment which shows regions of similarity and difference between DEX0455_051.nt.1 (SEQ ID NO:98; Ovr107) and DEX0455_051.nt.4 (SEQ ID NO:101);

FIGURE 14 is a nucleotide sequence alignment which shows regions of similarity and difference between DEX0455_051.nt.1 (SEQ ID NO:98; Ovr107) and DEX0455_051.nt.5 (SEQ ID NO:102);

FIGURE 15 is a nucleotide sequence alignment which shows regions of similarity and difference between DEX0455_051.nt.1 (SEQ ID NO:98; Ovr107) and DEX0455_051.nt.6 (SEQ ID NO:103; Ovr107v4);

FIGURE 16 is a nucleotide sequence alignment which shows regions of similarity and difference between DEX0455_053.nt.1 (SEQ ID NO:108; Ovr110) and DEX0455_053.nt.2 (SEQ ID NO:109; Ovr110v1);

FIGURE 17 is an amino acid sequence alignment which shows regions of similarity and difference between DEX0455_053.aa.1 (SEQ ID NO:268; Ovr110) and DEX0455_053.aa.2 (SEQ ID NO:269);

FIGURE 18 is an amino acid sequence alignment which shows regions of similarity and difference between DEX0455_053.aa.1 (SEQ ID NO:268; Ovr110) and DEX0455_053.aa.3 (SEQ ID NO:270).

DETAILED DESCRIPTION OF THE INVENTION

Definitions and General Techniques

Unless otherwise defined herein, scientific and technical terms used in connection with the present invention shall have the meanings that are commonly understood by those of ordinary skill in the art. Further, unless otherwise required by context, singular terms

shall include pluralities and plural terms shall include the singular. Generally, nomenclatures used in connection with, and techniques of, cell and tissue culture, molecular biology, immunology, microbiology, genetics and protein and nucleic acid chemistry and hybridization described herein are those well known and commonly used in the art. The methods and techniques of the present invention are generally performed according to conventional methods well known in the art and as described in various general and more specific references that are cited and discussed throughout the present specification unless otherwise indicated. *See, e.g.*, Sambrook *et al.*, Molecular Cloning: A Laboratory Manual, 2d ed., Cold Spring Harbor Laboratory Press (1989) and Sambrook *et al.*, Molecular Cloning: A Laboratory Manual, 3d ed., Cold Spring Harbor Press (2001); Ausubel *et al.*, Current Protocols in Molecular Biology, Greene Publishing Associates (1992, and Supplements to 2000); Ausubel *et al.*, Short Protocols in Molecular Biology: A Compendium of Methods from Current Protocols in Molecular Biology – 4th Ed., Wiley & Sons (1999); Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press (1990); and Harlow and Lane, Using Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press (1999).

Enzymatic reactions and purification techniques are performed according to manufacturer's specifications, as commonly accomplished in the art or as described herein. The nomenclatures used in connection with, and the laboratory procedures and techniques of, analytical chemistry, synthetic organic chemistry, and medicinal and pharmaceutical chemistry described herein are those well known and commonly used in the art. Standard techniques are used for chemical syntheses, chemical analyses, pharmaceutical preparation, formulation, and delivery, and treatment of patients.

The following terms, unless otherwise indicated, shall be understood to have the following meanings:

A "nucleic acid molecule" of this invention refers to a polymeric form of nucleotides and includes both sense and antisense strands of RNA, cDNA, genomic DNA, and synthetic forms and mixed polymers of the above. A nucleotide refers to a ribonucleotide, deoxynucleotide or a modified form of either type of nucleotide. A "nucleic acid molecule" as used herein is synonymous with "nucleic acid" and "polynucleotide." The term "nucleic acid molecule" usually refers to a molecule of at least 10 bases in length, unless otherwise specified. The term includes single- and double-stranded forms of DNA. In addition, a polynucleotide may include either or both naturally

occurring and modified nucleotides linked together by naturally occurring and/or non-naturally occurring nucleotide linkages.

Nucleotides are represented by single letter symbols in nucleic acid molecule sequences. The following table lists symbols identifying nucleotides or groups of nucleotides which may occupy the symbol position on a nucleic acid molecule. *See* Nomenclature Committee of the International Union of Biochemistry (NC-IUB), Nomenclature for incompletely specified bases in nucleic acid sequences, Recommendations 1984., *Eur J Biochem.* 150(1):1-5 (1985).

Symbol	Meaning	Group/Origin of Designation	Complementary Symbol
a	a	Adenine	t/u
g	g	Guanine	c
c	c	Cytosine	g
t	t	Thymine	a
u	u	Uracil	a
r	g or a	puRine	y
y	t/u or c	pYrimidine	r
m	a or c	aMino	k
k	g or t/u	Keto	m
s	g or c	Strong interactions 3H-bonds	w
w	a or t/u	Weak interactions 2H-bonds	s
b	g or c or t/u	not a	v
d	a or g or t/u	not c	h
h	a or c or t/u	not g	d
v	a or g or c	not t, not u	b
n	a or g or c or t/u, unknown, or other	aNy	n

The nucleic acid molecules may be modified chemically or biochemically or may contain non-natural or derivatized nucleotide bases, as will be readily appreciated by those of skill in the art. Such modifications include, for example, labels, methylation, substitution of one or more of the naturally occurring nucleotides with an analog, internucleotide modifications such as uncharged linkages (*e.g.*, methyl phosphonates, phosphotriesters, phosphoramidates, carbamates, etc.), charged linkages (*e.g.*, phosphorothioates, phosphorodithioates, etc.), pendent moieties (*e.g.*, polypeptides), intercalators (*e.g.*, acridine, psoralen, etc.), chelators, alkylators, and modified linkages (*e.g.*, alpha anomeric nucleic acids, etc.) The term "nucleic acid molecule" also includes any topological conformation, including single-stranded, double-stranded, partially duplexed, triplexed, hairpinned, circular and padlocked conformations. Also included are synthetic molecules that mimic polynucleotides in their ability to bind to a designated

sequence via hydrogen bonding and other chemical interactions. Such molecules are known in the art and include, for example, those in which peptide linkages substitute for phosphate linkages in the backbone of the molecule.

A "gene" is defined as a nucleic acid molecule that comprises a nucleic acid sequence that encodes a polypeptide and the expression control sequences that surround the nucleic acid sequence that encodes the polypeptide. For instance, a gene may comprise a promoter, one or more enhancers, a nucleic acid sequence that encodes a polypeptide, downstream regulatory sequences and, possibly, other nucleic acid sequences involved in regulation of the expression of an RNA. As is well known in the art, eukaryotic genes usually contain both exons and introns. The term "exon" refers to a nucleic acid sequence found in genomic DNA that is bioinformatically predicted and/or experimentally confirmed to contribute contiguous sequence to a mature mRNA transcript. The term "intron" refers to a nucleic acid sequence found in genomic DNA that is predicted and/or confirmed to not contribute to a mature mRNA transcript, but rather to be "spliced out" during processing of the transcript.

A nucleic acid molecule or polypeptide is "derived" from a particular species if the nucleic acid molecule or polypeptide has been isolated from the particular species, or if the nucleic acid molecule or polypeptide is homologous to a nucleic acid molecule or polypeptide isolated from a particular species.

An "isolated" or "substantially pure" nucleic acid or polynucleotide (*e.g.*, an RNA, DNA or a mixed polymer) is one which is substantially separated from other cellular components that naturally accompany the native polynucleotide in its natural host cell, *e.g.*, ribosomes, polymerases, or genomic sequences with which it is naturally associated. The term embraces a nucleic acid or polynucleotide that (1) has been removed from its naturally occurring environment, (2) is not associated with all or a portion of a polynucleotide in which the "isolated polynucleotide" is found in nature, (3) is operatively linked to a polynucleotide which it is not linked to in nature, (4) does not occur in nature as part of a larger sequence or (5) includes nucleotides or internucleoside bonds that are not found in nature. The term "isolated" or "substantially pure" also can be used in reference to recombinant or cloned DNA isolates, chemically synthesized polynucleotide analogs, or polynucleotide analogs that are biologically synthesized by heterologous systems. The term "isolated nucleic acid molecule" includes nucleic acid molecules that are integrated into a host cell chromosome at a heterologous site, recombinant fusions of a

native fragment to a heterologous sequence, recombinant vectors present as episomes or as integrated into a host cell chromosome.

A "part" of a nucleic acid molecule refers to a nucleic acid molecule that comprises a partial contiguous sequence of at least 10 bases of the reference nucleic acid molecule. Preferably, a part comprises at least 15 to 20 bases of a reference nucleic acid molecule. In theory, a nucleic acid sequence of 17 nucleotides is of sufficient length to occur at random less frequently than once in the three gigabase human genome, and thus provides a nucleic acid probe that can uniquely identify the reference sequence in a nucleic acid mixture of genomic complexity. A preferred part is one that comprises a nucleic acid sequence that can encode at least 6 contiguous amino acid sequences (fragments of at least 18 nucleotides) because they are useful in directing the expression or synthesis of peptides that are useful in mapping the epitopes of the polypeptide encoded by the reference nucleic acid. *See, e.g.*, Geysen *et al.*, *Proc. Natl. Acad. Sci. USA* 81:3998-4002 (1984); and U.S. Patent Nos. 4,708,871 and 5,595,915, the disclosures of which are incorporated herein by reference in their entireties. A part may also comprise at least 25, 30, 35 or 40 nucleotides of a reference nucleic acid molecule, or at least 50, 60, 70, 80, 90, 100, 150, 200, 250, 300, 350, 400 or 500 nucleotides of a reference nucleic acid molecule. A part of a nucleic acid molecule may comprise no other nucleic acid sequences. Alternatively, a part of a nucleic acid may comprise other nucleic acid sequences from other nucleic acid molecules.

The term "oligonucleotide" refers to a nucleic acid molecule generally comprising a length of 200 bases or fewer. The term often refers to single-stranded deoxyribonucleotides, but it can refer as well to single-or double-stranded ribonucleotides, RNA:DNA hybrids and double-stranded DNAs, among others. Preferably, oligonucleotides are 10 to 60 bases in length and most preferably 12, 13, 14, 15, 16, 17, 18, 19 or 20 bases in length. Other preferred oligonucleotides are 25, 30, 35, 40, 45, 50, 55 or 60 bases in length. Oligonucleotides may be single-stranded, *e.g.* for use as probes or primers, or may be double-stranded, *e.g.* for use in the construction of a mutant gene. Oligonucleotides of the invention can be either sense or antisense oligonucleotides. An oligonucleotide can be derivatized or modified as discussed above for nucleic acid molecules.

Oligonucleotides, such as single-stranded DNA probe oligonucleotides, often are synthesized by chemical methods, such as those implemented on automated

oligonucleotide synthesizers. However, oligonucleotides can be made by a variety of other methods, including in vitro recombinant DNA-mediated techniques and by expression of DNAs in cells and organisms. Initially, chemically synthesized DNAs typically are obtained without a 5' phosphate. The 5' ends of such oligonucleotides are not substrates for phosphodiester bond formation by ligation reactions that employ DNA ligases typically used to form recombinant DNA molecules. Where ligation of such oligonucleotides is desired, a phosphate can be added by standard techniques, such as those that employ a kinase and ATP. The 3' end of a chemically synthesized oligonucleotide generally has a free hydroxyl group and, in the presence of a ligase, such as T4 DNA ligase, readily will form a phosphodiester bond with a 5' phosphate of another polynucleotide, such as another oligonucleotide. As is well known, this reaction can be prevented selectively, where desired, by removing the 5' phosphates of the other polynucleotide(s) prior to ligation.

The term "naturally occurring nucleotide" referred to herein includes naturally occurring deoxyribonucleotides and ribonucleotides. The term "modified nucleotides" referred to herein includes nucleotides with modified or substituted sugar groups and the like. The term "nucleotide linkages" referred to herein includes nucleotide linkages such as phosphorothioate, phosphorodithioate, phosphoroselenoate, phosphorodiselenoate, phosphoroanilothioate, phoshoraniladate, phosphoroamidate, and the like. *See e.g.*, LaPlanche *et al. Nucl. Acids Res.* 14:9081-9093 (1986); Stein *et al. Nucl. Acids Res.* 16:3209-3221 (1988); Zon *et al. Anti-Cancer Drug Design* 6:539-568 (1991); Zon *et al.*, in Eckstein (ed.) Oligonucleotides and Analogues: A Practical Approach, pp. 87-108, Oxford University Press (1991); Uhlmann and Peyman *Chemical Reviews* 90:543 (1990), and U.S. Patent No. 5,151,510, the disclosure of which is hereby incorporated by reference in its entirety.

Unless specified otherwise, the left hand end of a polynucleotide sequence in sense orientation is the 5' end and the right hand end of the sequence is the 3' end. In addition, the left hand direction of a polynucleotide sequence in sense orientation is referred to as the 5' direction, while the right hand direction of the polynucleotide sequence is referred to as the 3' direction. Further, unless otherwise indicated, each nucleotide sequence is set forth herein as a sequence of deoxyribonucleotides. It is intended, however, that the given sequence be interpreted as would be appropriate to the polynucleotide composition: for

example, if the isolated nucleic acid is composed of RNA, the given sequence intends ribonucleotides, with uridine substituted for thymidine.

The term "allelic variant" refers to one of two or more alternative naturally occurring forms of a gene, wherein each gene possesses a unique nucleotide sequence. In a preferred embodiment, different alleles of a given gene have similar or identical biological properties.

The term "percent sequence identity" in the context of nucleic acid sequences refers to the residues in two sequences which are the same when aligned for maximum correspondence. The length of sequence identity comparison may be over a stretch of at least about nine nucleotides, usually at least about 20 nucleotides, more usually at least about 24 nucleotides, typically at least about 28 nucleotides, more typically at least about 32 nucleotides, and preferably at least about 36 or more nucleotides. There are a number of different algorithms known in the art which can be used to measure nucleotide sequence identity. For instance, polynucleotide sequences can be compared using FASTA, Gap or Bestfit, which are programs in Wisconsin Package Version 10.0, Genetics Computer Group (GCG), Madison, Wisconsin. FASTA, which includes, *e.g.*, the programs FASTA2 and FASTA3, provides alignments and percent sequence identity of the regions of the best overlap between the query and search sequences (Pearson, *Methods Enzymol.* 183: 63-98 (1990); Pearson, *Methods Mol. Biol.* 132: 185-219 (2000); Pearson, *Methods Enzymol.* 266: 227-258 (1996); Pearson, *J. Mol. Biol.* 276: 71-84 (1998)). Unless otherwise specified, default parameters for a particular program or algorithm are used. For instance, percent sequence identity between nucleic acid sequences can be determined using FASTA with its default parameters (a word size of 6 and the NOPAM factor for the scoring matrix) or using Gap with its default parameters as provided in GCG Version 6.1.

A reference to a nucleic acid sequence encompasses its complement unless otherwise specified. Thus, a reference to a nucleic acid molecule having a particular sequence should be understood to encompass its complementary strand, with its complementary sequence. The complementary strand is also useful, *e.g.*, for antisense therapy, double-stranded RNA (dsRNA) inhibition (RNAi), combination of triplex and antisense, hybridization probes and PCR primers.

In the molecular biology art, researchers use the terms "percent sequence identity", "percent sequence similarity" and "percent sequence homology" interchangeably. In this

application, these terms shall have the same meaning with respect to nucleic acid sequences only.

The term "substantial similarity" or "substantial sequence similarity," when referring to a nucleic acid or fragment thereof, indicates that, when optimally aligned with appropriate nucleotide insertions or deletions with another nucleic acid (or its complementary strand), there is nucleotide sequence identity in at least about 50%, more preferably 60% of the nucleotide bases, usually at least about 70%, more usually at least about 80%, preferably at least about 90%, and more preferably at least about 95-98% of the nucleotide bases, as measured by any well known algorithm of sequence identity, such as FASTA, BLAST or Gap, as discussed above.

Alternatively, substantial similarity exists between a first and second nucleic acid sequence when the first nucleic acid sequence or fragment thereof hybridizes to an antisense strand of the second nucleic acid, under selective hybridization conditions. Typically, selective hybridization will occur between the first nucleic acid sequence and an antisense strand of the second nucleic acid sequence when there is at least about 55% sequence identity between the first and second nucleic acid sequences— preferably at least about 65%, more preferably at least about 75%, and most preferably at least about 90% — over a stretch of at least about 14 nucleotides, more preferably at least 17 nucleotides, even more preferably at least 20, 25, 30, 35, 40, 50, 60, 70, 80, 90 or 100 nucleotides.

Nucleic acid hybridization will be affected by such conditions as salt concentration, temperature, solvents, the base composition of the hybridizing species, length of the complementary regions, and the number of nucleotide base mismatches between the hybridizing nucleic acids, as will be readily appreciated by those skilled in the art. "Stringent hybridization conditions" and "stringent wash conditions" in the context of nucleic acid hybridization experiments depend upon a number of different physical parameters. The most important parameters include temperature of hybridization, base composition of the nucleic acids, salt concentration and length of the nucleic acid. One having ordinary skill in the art knows how to vary these parameters to achieve a particular stringency of hybridization. In general, "stringent hybridization" is performed at about 25°C below the thermal melting point (T_m) for the specific DNA hybrid under a particular set of conditions. "Stringent washing" is performed at temperatures about 5°C lower than the T_m for the specific DNA hybrid under a particular set of conditions. The T_m is the

temperature at which 50% of the target sequence hybridizes to a perfectly matched probe. *See* Sambrook (1989), *supra*, p. 9.51.

The T_m for a particular DNA-DNA hybrid can be estimated by the formula:

$T_m = 81.5°C + 16.6 (\log_{10}[Na^+]) + 0.41$ (fraction G + C) – 0.63 (% formamide) - (600/l) where l is the length of the hybrid in base pairs.

The T_m for a particular RNA-RNA hybrid can be estimated by the formula:

$T_m = 79.8°C + 18.5 (\log_{10}[Na^+]) + 0.58$ (fraction G + C) + 11.8 (fraction G + C)^2 - 0.35 (% formamide) - (820/l).

The T_m for a particular RNA-DNA hybrid can be estimated by the formula:

$T_m = 79.8°C + 18.5(\log_{10}[Na^+]) + 0.58$ (fraction G + C) + 11.8 (fraction G + C)^2 - 0.50 (% formamide) - (820/l).

In general, the T_m decreases by 1-1.5°C for each 1% of mismatch between two nucleic acid sequences. Thus, one having ordinary skill in the art can alter hybridization and/or washing conditions to obtain sequences that have higher or lower degrees of sequence identity to the target nucleic acid. For instance, to obtain hybridizing nucleic acids that contain up to 10% mismatch from the target nucleic acid sequence, 10-15°C would be subtracted from the calculated T_m of a perfectly matched hybrid, and then the hybridization and washing temperatures adjusted accordingly. Probe sequences may also hybridize specifically to duplex DNA under certain conditions to form triplex or other higher order DNA complexes. The preparation of such probes and suitable hybridization conditions are well known in the art.

An example of stringent hybridization conditions for hybridization of complementary nucleic acid sequences having more than 100 complementary residues on a filter in a Southern or Northern blot or for screening a library is 50% formamide/6X SSC at 42°C for at least ten hours and preferably overnight (approximately 16 hours). Another example of stringent hybridization conditions is 6X SSC at 68°C without formamide for at least ten hours and preferably overnight. An example of moderate stringency hybridization conditions is 6X SSC at 55°C without formamide for at least ten hours and preferably overnight. An example of low stringency hybridization conditions for hybridization of complementary nucleic acid sequences having more than 100 complementary residues on a filter in a Southern or northern blot or for screening a library is 6X SSC at 42°C for at least ten hours. Hybridization conditions to identify nucleic acid sequences that are similar but not identical can be identified by experimentally changing

the hybridization temperature from 68°C to 42°C while keeping the salt concentration constant (6X SSC), or keeping the hybridization temperature and salt concentration constant (*e.g.* 42°C and 6X SSC) and varying the formamide concentration from 50% to 0%. Hybridization buffers may also include blocking agents to lower background. These agents are well known in the art. *See* Sambrook *et al.* (1989), *supra*, pages 8.46 and 9.46-9.58. *See also* Ausubel (1992), *supra*, Ausubel (1999), *supra*, and Sambrook (2001), *supra*.

Wash conditions also can be altered to change stringency conditions. An example of stringent wash conditions is a 0.2x SSC wash at 65°C for 15 minutes (*see* Sambrook (1989), *supra*, for SSC buffer). Often the high stringency wash is preceded by a low stringency wash to remove excess probe. An exemplary medium stringency wash for duplex DNA of more than 100 base pairs is 1x SSC at 45°C for 15 minutes. An exemplary low stringency wash for such a duplex is 4x SSC at 40°C for 15 minutes. In general, signal-to-noise ratio of 2x or higher than that observed for an unrelated probe in the particular hybridization assay indicates detection of a specific hybridization.

As defined herein, nucleic acids that do not hybridize to each other under stringent conditions are still substantially similar to one another if they encode polypeptides that are substantially identical to each other. This occurs, for example, when a nucleic acid is created synthetically or recombinantly using a high codon degeneracy as permitted by the redundancy of the genetic code.

Hybridization conditions for nucleic acid molecules that are shorter than 100 nucleotides in length (*e.g.*, for oligonucleotide probes) may be calculated by the formula:

$T_m = 81.5°C + 16.6(\log_{10}[Na^+]) + 0.41(\text{fraction G+C}) -(600/N)$, wherein N is change length and the $[Na^+]$ is 1 M or less. *See* Sambrook (1989), *supra*, p. 11.46. For hybridization of probes shorter than 100 nucleotides, hybridization is usually performed under stringent conditions (5-10°C below the T_m) using high concentrations (0.1-1.0 pmol/ml) of probe. *Id.* at p. 11.45. Determination of hybridization using mismatched probes, pools of degenerate probes or "guessmers," as well as hybridization solutions and methods for empirically determining hybridization conditions are well known in the art. *See, e.g.*, Ausubel (1999), *supra*; Sambrook (1989), *supra*, pp. 11.45-11.57.

The term "digestion" or "digestion of DNA" refers to catalytic cleavage of the DNA with a restriction enzyme that acts only at certain sequences in the DNA. The various restriction enzymes referred to herein are commercially available and their

reaction conditions, cofactors and other requirements for use are known and routine to the skilled artisan. For analytical purposes, typically, 1 μg of plasmid or DNA fragment is digested with about 2 units of enzyme in about 20 μl of reaction buffer. For the purpose of isolating DNA fragments for plasmid construction, typically 5 to 50 μg of DNA are digested with 20 to 250 units of enzyme in proportionately larger volumes. Appropriate buffers and substrate amounts for particular restriction enzymes are described in standard laboratory manuals, such as those referenced below, and are specified by commercial suppliers. Incubation times of about 1 hour at 37°C are ordinarily used, but conditions may vary in accordance with standard procedures, the supplier's instructions and the particulars of the reaction. After digestion, reactions may be analyzed, and fragments may be purified by electrophoresis through an agarose or polyacrylamide gel, using well known methods that are routine for those skilled in the art.

The term "ligation" refers to the process of forming phosphodiester bonds between two or more polynucleotides, which most often are double-stranded DNAs. Techniques for ligation are well known to the art and protocols for ligation are described in standard laboratory manuals and references, such as, *e.g.*, Sambrook (1989), *supra.*

Genome-derived "single exon probes," are probes that comprise at least part of an exon ("reference exon") and can hybridize detectably under high stringency conditions to transcript-derived nucleic acids that include the reference exon but do not hybridize detectably under high stringency conditions to nucleic acids that lack the reference exon. Single exon probes typically further comprise, contiguous to a first end of the exon portion, a first intronic and/or intergenic sequence that is identically contiguous to the exon in the genome, and may contain a second intronic and/or intergenic sequence that is identically contiguous to the exon in the genome. The minimum length of genome-derived single exon probes is defined by the requirement that the exonic portion be of sufficient length to hybridize under high stringency conditions to transcript-derived nucleic acids, as discussed above. The maximum length of genome-derived single exon probes is defined by the requirement that the probes contain portions of no more than one exon. The single exon probes may contain priming sequences not found in contiguity with the rest of the probe sequence in the genome, which priming sequences are useful for PCR and other amplification-based technologies. In another aspect, the invention is directed to single exon probes based on the OSNAs disclosed herein.

In one embodiment, the term "microarray" refers to a "nucleic acid microarray" having a substrate-bound plurality of nucleic acids, hybridization to each of the plurality of bound nucleic acids being separately detectable. The substrate can be solid or porous, planar or non-planar, unitary or distributed. Nucleic acid microarrays include all the devices so called in Schena (ed.), DNA Microarrays: A Practical Approach (Practical Approach Series), Oxford University Press (1999); *Nature Genet.* 21(1)(suppl.):1 - 60 (1999); Schena (ed.), Microarray Biochip: Tools and Technology, Eaton Publishing Company/BioTechniques Books Division (2000). Additionally, these nucleic acid microarrays include a substrate-bound plurality of nucleic acids in which the plurality of nucleic acids are disposed on a plurality of beads, rather than on a unitary planar substrate, as is described, *inter alia*, in Brenner *et al.*, *Proc. Natl. Acad. Sci. USA* 97(4):1665-1670 (2000). Examples of nucleic acid microarrays may be found in U.S. Patent Nos. 6,391,623, 6,383,754, 6,383,749, 6,380,377, 6,379,897, 6,376,191, 6,372,431, 6,351,712 6,344,316, 6,316,193, 6,312,906, 6,309,828, 6,309,824, 6,306,643, 6,300,063, 6,287,850, 6,284,497, 6,284,465, 6,280,954, 6,262,216, 6,251,601, 6,245,518, 6,263,287, 6,251,601, 6,238,866, 6,228,575, 6,214,587, 6,203,989, 6,171,797, 6,103,474, 6,083,726, 6,054,274, 6,040,138, 6,083,726, 6,004,755, 6,001,309, 5,958,342, 5,952,180, 5,936,731, 5,843,655, 5,814,454, 5,837,196, 5,436,327, 5,412,087, and 5,405,783, the disclosures of which are incorporated herein by reference in their entireties.

In an alternative embodiment, a "microarray" may also refer to a "peptide microarray" or "protein microarray" having a substrate-bound collection or plurality of polypeptides, the binding to each of the plurality of bound polypeptides being separately detectable. Alternatively, the peptide microarray may have a plurality of binders, including but not limited to monoclonal antibodies, polyclonal antibodies, phage display binders, yeast 2 hybrid binders, and aptamers, which can specifically detect the binding of the polypeptides of this invention. The array may be based on autoantibody detection to the polypeptides of this invention, see Robinson *et al., Nature Medicine* 8(3):295-301 (2002). Examples of peptide arrays may be found in WO 02/31463, WO 02/25288, WO 01/94946, WO 01/88162, WO 01/68671, WO 01/57259, WO 00/61806, WO 00/54046, WO 00/47774, WO 99/40434, WO 99/39210, and WO 97/42507 and U.S. Patent Nos. 6,268,210, 5,766,960, and 5,143,854, the disclosures of which are incorporated herein by reference in their entireties.

In addition, determination of the levels of the OSNA or OSP may be made in a multiplex manner using techniques described in WO 02/29109, WO 02/24959, WO 01/83502, WO01/73113, WO 01/59432, WO 01/57269, and WO 99/67641, the disclosures of which are incorporated herein by reference in their entireties.

The term "mutant", "mutated", or "mutation" when applied to nucleic acid sequences means that nucleotides in a nucleic acid sequence may be inserted, deleted or changed compared to a reference nucleic acid sequence. A single alteration may be made at a locus (a point mutation) or multiple nucleotides may be inserted, deleted or changed at a single locus. In addition, one or more alterations may be made at any number of loci within a nucleic acid sequence. In a preferred embodiment of the present invention, the nucleic acid sequence is the wild type nucleic acid sequence encoding an OSP or is an OSNA. The nucleic acid sequence may be mutated by any method known in the art including those mutagenesis techniques described *infra*.

The term "error-prone PCR" refers to a process for performing PCR under conditions where the copying fidelity of the DNA polymerase is low, such that a high rate of point mutations is obtained along the entire length of the PCR product. *See, e.g.*, Leung *et al.*, *Technique* 1: 11-15 (1989) and Caldwell *et al.*, *PCR Methods Applic.* 2: 28-33 (1992).

The term "oligonucleotide-directed mutagenesis" refers to a process which enables the generation of site-specific mutations in any cloned DNA segment of interest. *See, e.g.*, Reidhaar-Olson *et al.*, *Science* 241: 53-57 (1988).

The term "assembly PCR" refers to a process which involves the assembly of a PCR product from a mixture of small DNA fragments. A large number of different PCR reactions occur in parallel in the same vial, with the products of one reaction priming the products of another reaction.

The term "sexual PCR mutagenesis" or "DNA shuffling" refers to a method of error-prone PCR coupled with forced homologous recombination between DNA molecules of different but highly related DNA sequence *in vitro*, caused by random fragmentation of the DNA molecule based on sequence similarity, followed by fixation of the crossover by primer extension in an error-prone PCR reaction. *See, e.g.*, Stemmer, *Proc. Natl. Acad. Sci. U.S.A.* 91: 10747-10751 (1994). DNA shuffling can be carried out between several related genes ("Family shuffling").

The term "*in vivo* mutagenesis" refers to a process of generating random mutations in any cloned DNA of interest which involves the propagation of the DNA in a strain of bacteria such as *E. coli* that carries mutations in one or more of the DNA repair pathways. These "mutator" strains have a higher random mutation rate than that of a wild-type parent. Propagating the DNA in a mutator strain will eventually generate random mutations within the DNA.

The term "cassette mutagenesis" refers to any process for replacing a small region of a double-stranded DNA molecule with a synthetic oligonucleotide "cassette" that differs from the native sequence. The oligonucleotide often contains completely and/or partially randomized native sequence.

The term "recursive ensemble mutagenesis" refers to an algorithm for protein engineering (protein mutagenesis) developed to produce diverse populations of phenotypically related mutants whose members differ in amino acid sequence. This method uses a feedback mechanism to control successive rounds of combinatorial cassette mutagenesis. *See, e.g.*, Arkin *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* 89: 7811-7815 (1992).

The term "exponential ensemble mutagenesis" refers to a process for generating combinatorial libraries with a high percentage of unique and functional mutants, wherein small groups of residues are randomized in parallel to identify, at each altered position, amino acids which lead to functional proteins. *See, e.g.*, Delegrave *et al.*, *Biotechnology Research* 11: 1548-1552 (1993); Arnold, *Current Opinion in Biotechnology* 4: 450-455 (1993).

"Operatively linked" expression control sequences refers to a linkage in which the expression control sequence is either contiguous with the gene of interest to control the gene of interest, or acts in *trans* or at a distance to control the gene of interest.

The term "expression control sequence" as used herein refers to polynucleotide sequences which are necessary to affect the expression of coding sequences to which they are operatively linked. Expression control sequences are sequences which control the transcription, post-transcriptional events and translation of nucleic acid sequences. Expression control sequences include appropriate transcription initiation, termination, promoter and enhancer sequences; efficient RNA processing signals such as splicing and polyadenylation signals; sequences that stabilize cytoplasmic mRNA; sequences that enhance translation efficiency (*e.g.*, ribosome binding sites); sequences that enhance protein stability; and when desired, sequences that enhance protein secretion. The nature

of such control sequences differs depending upon the host organism; in prokaryotes, such control sequences generally include promoter, ribosomal binding site, and transcription termination sequence. The term "control sequences" is intended to include, at a minimum, all components whose presence is essential for expression, and can also include additional components whose presence is advantageous, for example, leader sequences and fusion partner sequences.

The term "vector," as used herein, is intended to refer to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a "plasmid", which refers to a circular double-stranded DNA loop into which additional DNA segments may be ligated. Other vectors include cosmids, bacterial artificial chromosomes (BAC) and yeast artificial chromosomes (YAC). Another type of vector is a viral vector, wherein additional DNA segments may be ligated into the viral genome. Viral vectors that infect bacterial cells are referred to as bacteriophages. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (*e.g.*, bacterial vectors having a bacterial origin of replication). Other vectors can be integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors are capable of directing the expression of genes to which they are operatively linked. Such vectors are referred to herein as "recombinant expression vectors" (or simply, "expression vectors"). In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids. In the present specification, "plasmid" and "vector" may be used interchangeably as the plasmid is the most commonly used form of vector. However, the invention is intended to include other forms of expression vectors that serve equivalent functions.

The term "recombinant host cell" (or simply "host cell"), as used herein, is intended to refer to a cell into which a recombinant expression vector has been introduced. It should be understood that such terms are intended to refer not only to the particular subject cell but to the progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term "host cell" as used herein.

As used herein, the phrase "open reading frame" and the equivalent acronym "ORF" refers to that portion of a transcript-derived nucleic acid that can be translated in its

entirety into a sequence of contiguous amino acids. As so defined, an ORF has length, measured in nucleotides, exactly divisible by 3. As so defined, an ORF need not encode the entirety of a natural protein.

As used herein, the phrase "ORF-encoded peptide" refers to the predicted or actual translation of an ORF.

As used herein, the phrase "degenerate variant" of a reference nucleic acid sequence is meant to be inclusive of all nucleic acid sequences that can be directly translated, using the standard genetic code, to provide an amino acid sequence identical to that translated from the reference nucleic acid sequence.

The term "polypeptide" encompasses both naturally occurring and non-naturally occurring proteins and polypeptides, as well as polypeptide fragments and polypeptide mutants, derivatives and analogs thereof. A polypeptide may be monomeric or polymeric. Further, a polypeptide may comprise a number of different modules within a single polypeptide each of which has one or more distinct activities. A preferred polypeptide in accordance with the invention comprises an OSP encoded by a nucleic acid molecule of the instant invention, or a fragment, mutant, analog or derivative thereof.

The term "isolated protein" or "isolated polypeptide" is a protein or polypeptide that by virtue of its origin or source of derivation (1) is not associated with naturally associated components that accompany it in its native state, (2) is free of other proteins from the same species (3) is expressed by a cell from a different species, or (4) does not occur in nature. Thus, a polypeptide that is chemically synthesized or synthesized in a cellular system different from the cell from which it naturally originates will be "isolated" from its naturally associated components. A polypeptide or protein may also be rendered substantially free of naturally associated components by isolation, using protein purification techniques well known in the art.

A protein or polypeptide is "substantially pure," "substantially homogeneous" or "substantially purified" when at least about 60% to 75% of a sample exhibits a single species of polypeptide. The polypeptide or protein may be monomeric or multimeric. A substantially pure polypeptide or protein will typically comprise about 50%, 60%, 70%, 80% or 90% W/W of a protein sample, more usually about 95%, and preferably will be over 99% pure. Protein purity or homogeneity may be determined by a number of means well known in the art, such as polyacrylamide gel electrophoresis of a protein sample, followed by visualizing a single polypeptide band upon staining the gel with a stain well

known in the art. For certain purposes, higher resolution may be provided by using HPLC or other means well known in the art for purification.

The term "fragment" when used herein with respect to polypeptides of the present invention refers to a polypeptide that has an amino-terminal and/or carboxy-terminal deletion compared to a full-length OSP. In a preferred embodiment, the fragment is a contiguous sequence in which the amino acid sequence of the fragment is identical to the corresponding positions in the naturally occurring polypeptide. Fragments typically are at least 5, 6, 7, 8, 9 or 10 amino acids long, preferably at least 12, 14, 16 or 18 amino acids long, more preferably at least 20 amino acids long, more preferably at least 25, 30, 35, 40 or 45, amino acids, even more preferably at least 50 or 60 amino acids long, and even more preferably at least 70 amino acids long.

A "derivative" when used herein with respect to polypeptides of the present invention refers to a polypeptide which is substantially similar in primary structural sequence to an OSP but which includes, *e.g.*, *in vivo* or *in vitro* chemical and biochemical modifications that are not found in the OSP. Such modifications include, for example, acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphotidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cystine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. Other modifications include, *e.g.*, labeling with radionuclides, and various enzymatic modifications, as will be readily appreciated by those skilled in the art. A variety of methods for labeling polypeptides and of substituents or labels useful for such purposes are well known in the art, and include radioactive isotopes such as ^{125}I, ^{32}P, ^{35}S, ^{14}C and ^{3}H, ligands which bind to labeled antiligands (*e.g.*, antibodies), fluorophores, chemiluminescent agents, enzymes, and antiligands which can serve as specific binding pair members for a labeled ligand. The choice of label depends on the sensitivity required, ease of conjugation with the primer, stability requirements, and available instrumentation.

Methods for labeling polypeptides are well known in the art. *See* Ausubel (1992), *supra*; Ausubel (1999), *supra*.

The term "fusion protein" refers to polypeptides of the present invention coupled to a heterologous amino acid sequence. Fusion proteins are useful because they can be constructed to contain two or more desired functional elements from two or more different proteins. A fusion protein comprises at least 10 contiguous amino acids from a polypeptide of interest, more preferably at least 20 or 30 amino acids, even more preferably at least 40, 50 or 60 amino acids, yet more preferably at least 75, 100 or 125 amino acids. Fusion proteins can be produced recombinantly by constructing a nucleic acid sequence that encodes the polypeptide or a fragment thereof in frame with a nucleic acid sequence encoding a different protein or peptide and then expressing the fusion protein. Alternatively, a fusion protein can be produced chemically by crosslinking the polypeptide or a fragment thereof to another protein.

The term "analog" refers to both polypeptide analogs and non-peptide analogs. The term "polypeptide analog" as used herein refers to a polypeptide that is comprised of a segment of at least 25 amino acids that has substantial identity to a portion of an amino acid sequence but which contains non-natural amino acids or non-natural inter-residue bonds. In a preferred embodiment, the analog has the same or similar biological activity as the native polypeptide. Typically, polypeptide analogs comprise a conservative amino acid substitution (or insertion or deletion) with respect to the naturally occurring sequence. Analogs typically are at least 20 amino acids long, preferably at least 50 amino acids long or longer, and can often be as long as a full-length naturally occurring polypeptide.

The term "non-peptide analog" refers to a compound with properties that are analogous to those of a reference polypeptide. A non-peptide compound may also be termed a "peptide mimetic" or a "peptidomimetic." Such compounds are often developed with the aid of computerized molecular modeling. Peptide mimetics that are structurally similar to useful peptides may be used to produce an equivalent effect. Generally, peptidomimetics are structurally similar to a paradigm polypeptide (*i.e.*, a polypeptide that has a desired biochemical property or pharmacological activity), but have one or more peptide linkages optionally replaced by a linkage selected from the group consisting of: --CH_2NH--, --CH_2S--, --CH_2-CH_2--, --CH=CH--(cis and trans), --$COCH_2$--, --$CH(OH)CH_2$--, and –CH_2SO--, by methods well known in the art. Systematic

substitution of one or more amino acids of a consensus sequence with a D-amino acid of the same type (*e.g.*, D-lysine in place of L-lysine) may also be used to generate more stable peptides. In addition, constrained peptides comprising a consensus sequence or a substantially identical consensus sequence variation may be generated by methods known in the art (Rizo *et al., Ann. Rev. Biochem.* 61:387-418 (1992)). For example, one may add internal cysteine residues capable of forming intramolecular disulfide bridges which cyclize the peptide.

The term "mutant" or "mutein" when referring to a polypeptide of the present invention relates to an amino acid sequence containing substitutions, insertions or deletions of one or more amino acids compared to the amino acid sequence of an OSP. A mutein may have one or more amino acid point substitutions, in which a single amino acid at a position has been changed to another amino acid, one or more insertions and/or deletions, in which one or more amino acids are inserted or deleted, respectively, in the sequence of the naturally occurring protein, and/or truncations of the amino acid sequence at either or both the amino or carboxy termini. Further, a mutein may have the same or different biological activity as the naturally occurring protein. For instance, a mutein may have an increased or decreased biological activity. A mutein has at least 50% sequence similarity to the wild type protein, preferred is 60% sequence similarity, more preferred is 70% sequence similarity. Even more preferred are muteins having 80%, 85% or 90% sequence similarity to an OSP. In an even more preferred embodiment, a mutein exhibits 95% sequence identity, even more preferably 97%, even more preferably 98% and even more preferably 99%. Sequence similarity may be measured by any common sequence analysis algorithm, such as GAP or BESTFIT or other variation Smith-Waterman alignment. *See*, T. F. Smith and M. S. Waterman, J. Mol. Biol. 147:195-197 (1981) and W.R. Pearson, Genomics 11:635-650 (1991).

Preferred amino acid substitutions are those which: (1) reduce susceptibility to proteolysis, (2) reduce susceptibility to oxidation, (3) alter binding affinity for forming protein complexes, (4) alter binding affinity or enzymatic activity, and (5) confer or modify other physicochemical or functional properties of such analogs. For example, single or multiple amino acid substitutions (preferably conservative amino acid substitutions) may be made in the naturally occurring sequence (preferably in the portion of the polypeptide outside the domain(s) forming intermolecular contacts. In a preferred embodiment, the amino acid substitutions are moderately conservative substitutions or

conservative substitutions. In a more preferred embodiment, the amino acid substitutions are conservative substitutions. A conservative amino acid substitution should not substantially change the structural characteristics of the parent sequence (*e.g.*, a replacement amino acid should not tend to disrupt a helix that occurs in the parent sequence, or disrupt other types of secondary structure that characterize the parent sequence). Examples of art-recognized polypeptide secondary and tertiary structures are described in Creighton (ed.), Proteins, Structures and Molecular Principles, W. H. Freeman and Company (1984); Branden *et al.* (ed.), Introduction to Protein Structure, Garland Publishing (1991); Thornton *et al.*, *Nature* 354:105-106 (1991).

As used herein, the twenty conventional amino acids and their abbreviations follow conventional usage. *See* Golub *et al.* (eds.), Immunology - A Synthesis 2nd Ed., Sinauer Associates (1991). Stereoisomers (*e.g.*, D-amino acids) of the twenty conventional amino acids, unnatural amino acids such as α-, α-disubstituted amino acids, N-alkyl amino acids, and other unconventional amino acids may also be suitable components for polypeptides of the present invention. Examples of unconventional amino acids include: 4-hydroxyproline, γ-carboxyglutamate, ε-N,N,N-trimethyllysine, ε-N-acetyllysine, O-phosphoserine, N-acetylserine, N-formylmethionine, 3-methylhistidine, 5-hydroxylysine, s-N-methylarginine, and other similar amino acids and imino acids (*e.g.*, 4-hydroxyproline). In the polypeptide notation used herein, the lefthand direction is the amino terminal direction and the right hand direction is the carboxy-terminal direction, in accordance with standard usage and convention.

By "homology" or "homologous" when referring to a polypeptide of the present invention it is meant polypeptides from different organisms with a similar sequence to the encoded amino acid sequence of an OSP and a similar biological activity or function. Although two polypeptides are said to be "homologous," this does not imply that there is necessarily an evolutionary relationship between the polypeptides. Instead, the term "homologous" is defined to mean that the two polypeptides have similar amino acid sequences and similar biological activities or functions. In a preferred embodiment, a homologous polypeptide is one that exhibits 50% sequence similarity to OSP, preferred is 60% sequence similarity, more preferred is 70% sequence similarity. Even more preferred are homologous polypeptides that exhibit 80%, 85% or 90% sequence similarity to an OSP. In yet a more preferred embodiment, a homologous polypeptide exhibits 95%, 97%, 98% or 99% sequence similarity.

When "sequence similarity" is used in reference to polypeptides, it is recognized that residue positions that are not identical often differ by conservative amino acid substitutions. In a preferred embodiment, a polypeptide that has "sequence similarity" comprises conservative or moderately conservative amino acid substitutions. A "conservative amino acid substitution" is one in which an amino acid residue is substituted by another amino acid residue having a side chain (R group) with similar chemical properties (*e.g.*, charge or hydrophobicity). In general, a conservative amino acid substitution will not substantially change the functional properties of a protein. In cases where two or more amino acid sequences differ from each other by conservative substitutions, the percent sequence identity or degree of similarity may be adjusted upwards to correct for the conservative nature of the substitution. Means for making this adjustment are well known to those of skill in the art. *See, e.g.*, Pearson, *Methods Mol. Biol.* 24: 307-31 (1994).

For instance, the following six groups each contain amino acids that are conservative substitutions for one another:

1) Serine (S), Threonine (T);
2) Aspartic Acid (D), Glutamic Acid (E);
3) Asparagine (N), Glutamine (Q);
4) Arginine (R), Lysine (K);
5) Isoleucine (I), Leucine (L), Methionine (M), Alanine (A), Valine (V), and
6) Phenylalanine (F), Tyrosine (Y), Tryptophan (W).

Alternatively, a conservative replacement is any change having a positive value in the PAM250 log-likelihood matrix disclosed in Gonnet *et al.*, *Science* 256: 1443-45 (1992). A "moderately conservative" replacement is any change having a nonnegative value in the PAM250 log-likelihood matrix.

Sequence similarity for polypeptides, which is also referred to as sequence identity, is typically measured using sequence analysis software. Protein analysis software matches similar sequences using measures of similarity assigned to various substitutions, deletions and other modifications, including conservative amino acid substitutions. For instance, GCG contains programs such as "Gap" and "Bestfit" which can be used with default parameters to determine sequence homology or sequence identity between closely related polypeptides, such as homologous polypeptides from different species of

organisms or between a wild type protein and a mutein thereof. *See, e.g.*, GCG Version 6.1. Other programs include FASTA, discussed *supra*.

A preferred algorithm when comparing a sequence of the invention to a database containing a large number of sequences from different organisms is the computer program BLAST, especially blastp or tblastn. *See, e.g.,* Altschul *et al.*, *J. Mol. Biol.* 215: 403-410 (1990); Altschul *et al.*, *Nucleic Acids Res.* 25:3389-402 (1997). Preferred parameters for blastp are:

Expectation value:	10 (default)
Filter:	seg (default)
Cost to open a gap:	11 (default)
Cost to extend a gap:	1 (default
Max. alignments:	100 (default)
Word size:	11 (default)
No. of descriptions:	100 (default)
Penalty Matrix:	BLOSUM62

The length of polypeptide sequences compared for homology will generally be at least about 16 amino acid residues, usually at least about 20 residues, more usually at least about 24 residues, typically at least about 28 residues, and preferably more than about 35 residues. When searching a database containing sequences from a large number of different organisms, it is preferable to compare amino acid sequences.

Algorithms other than blastp for database searching using amino acid sequences are known in the art. For instance, polypeptide sequences can be compared using FASTA, a program in GCG Version 6.1. FASTA (*e.g.*, FASTA2 and FASTA3) provides alignments and percent sequence identity of the regions of the best overlap between the query and search sequences (Pearson (1990), *supra*; Pearson (2000), *supra*. For example, percent sequence identity between amino acid sequences can be determined using FASTA with its default or recommended parameters (a word size of 2 and the PAM250 scoring matrix), as provided in GCG Version 6.1.

An "antibody" refers to an intact immunoglobulin, or to an antigen-binding portion thereof that competes with the intact antibody for specific binding to a molecular species, *e.g.*, a polypeptide of the instant invention. Antigen-binding portions may be produced by recombinant DNA techniques or by enzymatic or chemical cleavage of intact antibodies. Antigen-binding portions include, *inter alia*, Fab, Fab', $F(ab')_2$, Fv, dAb, and

complementarity determining region (CDR) fragments, single-chain antibodies (scFv), chimeric antibodies, diabodies and polypeptides that contain at least a portion of an immunoglobulin that is sufficient to confer specific antigen binding to the polypeptide. A Fab fragment is a monovalent fragment consisting of the VL, VH, CL and CH1 domains; a $F(ab')_2$ fragment is a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; a Fd fragment consists of the VH and CH1 domains; a Fv fragment consists of the VL and VH domains of a single arm of an antibody; and a dAb fragment consists of a VH domain. *See, e.g.,* Ward *et al.*, *Nature* 341: 544-546 (1989).

By "bind specifically" and "specific binding" as used herein it is meant the ability of the antibody to bind to a first molecular species in preference to binding to other molecular species with which the antibody and first molecular species are admixed. An antibody is said to "recognize" a first molecular species when it can bind specifically to that first molecular species.

A single-chain antibody (scFv) is an antibody in which VL and VH regions are paired to form a monovalent molecule via a synthetic linker that enables them to be made as a single protein chain. *See, e.g.,* Bird *et al.*, *Science* 242: 423-426 (1988); Huston *et al.*, *Proc. Natl. Acad. Sci. USA* 85: 5879-5883 (1988). Diabodies are bivalent, bispecific antibodies in which VH and VL domains are expressed on a single polypeptide chain, but using a linker that is too short to allow for pairing between the two domains on the same chain, thereby forcing the domains to pair with complementary domains of another chain and creating two antigen binding sites. *See e.g.*, Holliger *et al.*, *Proc. Natl. Acad. Sci. USA* 90: 6444-6448 (1993); Poljak *et al.*, *Structure* 2: 1121-1123 (1994). One or more CDRs may be incorporated into a molecule either covalently or noncovalently to make it an immunoadhesin. An immunoadhesin may incorporate the CDR(s) as part of a larger polypeptide chain, may covalently link the CDR(s) to another polypeptide chain, or may incorporate the CDR(s) noncovalently. The CDRs permit the immunoadhesin to specifically bind to a particular antigen of interest. A chimeric antibody is an antibody that contains one or more regions from one antibody and one or more regions from one or more other antibodies.

An antibody may have one or more binding sites. If there is more than one binding site, the binding sites may be identical to one another or may be different. For instance, a naturally occurring immunoglobulin has two identical binding sites, a single-chain

antibody or Fab fragment has one binding site, while a "bispecific" or "bifunctional" antibody has two different binding sites.

An "isolated antibody" is an antibody that (1) is not associated with naturally-associated components, including other naturally-associated antibodies, that accompany it in its native state, (2) is free of other proteins from the same species, (3) is expressed by a cell from a different species, or (4) does not occur in nature. It is known that purified proteins, including purified antibodies, may be stabilized with non-naturally-associated components. The non-naturally-associated component may be a protein, such as albumin (*e.g.*, BSA) or a chemical such as polyethylene glycol (PEG).

A "neutralizing antibody" or "an inhibitory antibody" is an antibody that inhibits the activity of a polypeptide or blocks the binding of a polypeptide to a ligand that normally binds to it. An "activating antibody" is an antibody that increases the activity of a polypeptide.

The term "epitope" includes any protein determinant capable of specific binding to an immunoglobulin or T-cell receptor. Epitopic determinants usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains and usually have specific three-dimensional structural characteristics, as well as specific charge characteristics. An antibody is said to specifically bind an antigen when the dissociation constant is less than1 μM, preferably less than100 nM and most preferably less than 10 nM.

The term "patient" includes human and veterinary subjects.

Throughout this specification and claims, the word "comprise," or variations such as "comprises" or "comprising," will be understood to imply the inclusion of a stated integer or group of integers but not the exclusion of any other integer or group of integers.

The term "ovarian specific" refers to a nucleic acid molecule or polypeptide that is expressed predominantly in the ovarian as compared to other tissues in the body. In a preferred embodiment, a "ovarian specific" nucleic acid molecule or polypeptide is detected at a level that is 1.5-fold higher than any other tissue in the body. In a more preferred embodiment, the "ovarian specific" nucleic acid molecule or polypeptide is detected at a level that is 2-fold higher than any other tissue in the body, more preferably 5-fold higher, still more preferably at least 10-fold, 15-fold, 20-fold, 25-fold, 50-fold or 100-fold higher than any other tissue in the body. Nucleic acid molecule levels may be measured by nucleic acid hybridization, such as Northern blot hybridization, or

quantitative PCR. Polypeptide levels may be measured by any method known to accurately quantitate protein levels, such as Western blot analysis.

Nucleic Acid Molecules, Regulatory Sequences, Vectors, Host Cells and Recombinant Methods of Making Polypeptides

Nucleic Acid Molecules

One aspect of the invention provides isolated nucleic acid molecules that are specific to the ovarian or to ovarian cells or tissue or that are derived from such nucleic acid molecules. These isolated ovarian specific nucleic acids (OSNAs) may comprise cDNA genomic DNA, RNA, or a combination thereof, a fragment of one of these nucleic acids, or may be a non-naturally occurring nucleic acid molecule. An OSNA may be derived from an animal. In a preferred embodiment, the OSNA is derived from a human or other mammal. In a more preferred embodiment, the OSNA is derived from a human or other primate. In an even more preferred embodiment, the OSNA is derived from a human.

In a preferred embodiment, the nucleic acid molecule encodes a polypeptide that is specific to ovarian, an ovarian-specific polypeptide (OSP). In a more preferred embodiment, the nucleic acid molecule encodes a polypeptide that comprises an amino acid sequence of SEQ ID NO: 129-295. In another highly preferred embodiment, the nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 1-128. Nucleotide sequences of the instantly-described nucleic acid molecules were determined by assembling several DNA molecules from either public or proprietary databases. Some of the underlying DNA sequences are the result, directly or indirectly, of at least one enzymatic polymerization reaction (*e.g.*, reverse transcription and/or polymerase chain reaction) using an automated sequencer (such as the MegaBACE™ 1000, Amersham Biosciences, Sunnyvale, CA, USA).

Nucleic acid molecules of the present invention may also comprise sequences that selectively hybridize to a nucleic acid molecule encoding an OSNA or a complement or antisense thereof. The hybridizing nucleic acid molecule may or may not encode a polypeptide or may or may not encode an OSP. However, in a preferred embodiment, the hybridizing nucleic acid molecule encodes an OSP. In a more preferred embodiment, the invention provides a nucleic acid molecule that selectively hybridizes to a nucleic acid molecule or the antisense sequence of a nucleic acid molecule that encodes a polypeptide

comprising an amino acid sequence of SEQ ID NO: 129-295. In an even more preferred embodiment, the invention provides a nucleic acid molecule that selectively hybridizes to a nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO: 1-128 or the antisense sequence thereof. Preferably, the nucleic acid molecule selectively hybridizes to a nucleic acid molecule or the antisense sequence of a nucleic acid molecule encoding an OSP under low stringency conditions. More preferably, the nucleic acid molecule selectively hybridizes to a nucleic acid molecule or the antisense sequence of a nucleic acid molecule encoding an OSP under moderate stringency conditions. Most preferably, the nucleic acid molecule selectively hybridizes to a nucleic acid molecule or the antisense sequence of a nucleic acid molecule encoding an OSP under high stringency conditions. In a preferred embodiment, the nucleic acid molecule hybridizes under low, moderate or high stringency conditions to a nucleic acid molecule or the antisense sequence of a nucleic acid molecule encoding a polypeptide comprising an amino acid sequence of SEQ ID NO: 129-295. In a more preferred embodiment, the nucleic acid molecule hybridizes under low, moderate or high stringency conditions to a nucleic acid molecule or the antisense sequence of a nucleic acid molecule comprising a nucleic acid sequence selected from SEQ ID NO: 1-128.

Nucleic acid molecules of the present invention may also comprise nucleic acid sequences that exhibit substantial sequence similarity to a nucleic acid encoding an OSP or a complement of the encoding nucleic acid molecule. In this embodiment, it is preferred that the nucleic acid molecule exhibit substantial sequence similarity to a nucleic acid molecule encoding human OSP. More preferred is a nucleic acid molecule exhibiting substantial sequence similarity to a nucleic acid molecule encoding a polypeptide having an amino acid sequence of SEQ ID NO: 129-295. By substantial sequence similarity it is meant a nucleic acid molecule having at least 60%, more preferably at least 70%, even more preferably at least 80% and even more preferably at least 85% sequence identity with a nucleic acid molecule encoding an OSP, such as a polypeptide having an amino acid sequence of SEQ ID NO: 129-295. In a more preferred embodiment, the similar nucleic acid molecule is one that has at least 90%, more preferably at least 95%, more preferably at least 97%, even more preferably at least 98%, and still more preferably at least 99% sequence identity with a nucleic acid molecule encoding an OSP. Most preferred in this embodiment is a nucleic acid molecule that has at least 99.5%, 99.6%, 99.7%, 99.8% or 99.9% sequence identity with a nucleic acid molecule encoding an OSP.

The nucleic acid molecules of the present invention are also inclusive of those exhibiting substantial sequence similarity to an OSNA or its complement. In this embodiment, it is preferred that the nucleic acid molecule exhibit substantial sequence similarity to a nucleic acid molecule having a nucleic acid sequence of SEQ ID NO: 1-128. By substantial sequence similarity it is meant a nucleic acid molecule that has at least 60%, more preferably at least 70%, even more preferably at least 80% and even more preferably at least 85% sequence identity with an OSNA, such as one having a nucleic acid sequence of SEQ ID NO: 1-128. More preferred is a nucleic acid molecule that has at least 90%, more preferably at least 95%, more preferably at least 97%, even more preferably at least 98%, and still more preferably at least 99% sequence identity with an OSNA. Most preferred is a nucleic acid molecule that has at least 99.5%, 99.6%, 99.7%, 99.8% or 99.9% sequence identity with an OSNA.

Nucleic acid molecules that exhibit substantial sequence similarity are inclusive of sequences that exhibit sequence identity over their entire length to an OSNA or to a nucleic acid molecule encoding an OSP, as well as sequences that are similar over only a part of its length. In this case, the part is at least 50 nucleotides of the OSNA or the nucleic acid molecule encoding an OSP, preferably at least 100 nucleotides, more preferably at least 150 or 200 nucleotides, even more preferably at least 250 or 300 nucleotides, still more preferably at least 400 or 500 nucleotides.

The substantially similar nucleic acid molecule may be a naturally occurring one that is derived from another species, especially one derived from another primate, wherein the similar nucleic acid molecule encodes an amino acid sequence that exhibits significant sequence identity to that of SEQ ID NO: 129-295 or demonstrates significant sequence identity to the nucleotide sequence of SEQ ID NO: 1-128. The similar nucleic acid molecule may also be a naturally occurring nucleic acid molecule from a human, when the OSNA is a member of a gene family. The similar nucleic acid molecule may also be a naturally occurring nucleic acid molecule derived from a non-primate, mammalian species, including without limitation, domesticated species, *e.g.*, dog, cat, mouse, rat, rabbit, hamster, cow, horse and pig; and wild animals, *e.g.*, monkey, fox, lions, tigers, bears, giraffes, zebras, etc. The substantially similar nucleic acid molecule may also be a naturally occurring nucleic acid molecule derived from a non-mammalian species, such as birds or reptiles. The naturally occurring substantially similar nucleic acid molecule may be isolated directly from humans or other species. In another embodiment, the

substantially similar nucleic acid molecule may be one that is experimentally produced by random mutation of a nucleic acid molecule. In another embodiment, the substantially similar nucleic acid molecule may be one that is experimentally produced by directed mutation of an OSNA. In a preferred embodiment, the substantially similar nucleic acid molecule is an OSNA.

The nucleic acid molecules of the present invention are also inclusive of allelic variants of an OSNA or a nucleic acid encoding an OSP. For example, single nucleotide polymorphisms (SNPs) occur frequently in eukaryotic genomes and the sequence determined from one individual of a species may differ from other allelic forms present within the population. More than 1.4 million SNPs have already been identified in the human genome, International Human Genome Sequencing Consortium, *Nature* 409: 860-921 (2001) – Variants with small deletions and insertions of more than a single nucleotide are also found in the general population, and often do not alter the function of the protein. In addition, amino acid substitutions occur frequently among natural allelic variants, and often do not substantially change protein function.

In a preferred embodiment, the allelic variant is a variant of a gene, wherein the gene is transcribed into a mRNA that encodes an OSP. In a more preferred embodiment, the gene is transcribed into a mRNA that encodes an OSP comprising an amino acid sequence of SEQ ID NO: 129-295. In another preferred embodiment, the allelic variant is a variant of a gene, wherein the gene is transcribed into a mRNA that is an OSNA. In a more preferred embodiment, the gene is transcribed into a mRNA that comprises the nucleic acid sequence of SEQ ID NO: 1-128. Also preferred is that the allelic variant be a naturally occurring allelic variant in the species of interest, particularly human.

Nucleic acid molecules of the present invention are also inclusive of nucleic acid sequences comprising a part of a nucleic acid sequence of the instant invention. The part may or may not encode a polypeptide, and may or may not encode a polypeptide that is an OSP. In a preferred embodiment, the part encodes an OSP. In one embodiment, the nucleic acid molecule comprises a part of an OSNA. In another embodiment, the nucleic acid molecule comprises a part of a nucleic acid molecule that hybridizes or exhibits substantial sequence similarity to an OSNA. In another embodiment, the nucleic acid molecule comprises a part of a nucleic acid molecule that is an allelic variant of an OSNA. In yet another embodiment, the nucleic acid molecule comprises a part of a nucleic acid molecule that encodes an OSP. A part comprises at least 10 nucleotides, more preferably

at least 15, 17, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250, 300, 350, 400 or 500 nucleotides. The maximum size of a nucleic acid part is one nucleotide shorter than the sequence of the nucleic acid molecule encoding the full-length protein.

Nucleic acid molecules of the present invention are also inclusive of nucleic acid sequences that encode fusion proteins, homologous proteins, polypeptide fragments, muteins and polypeptide analogs, as described *infra*.

Nucleic acid molecules of the present invention are also inclusive of nucleic acid sequences containing modifications of the native nucleic acid molecule. Examples of such modifications include, but are not limited to, nonnative internucleoside bonds, post-synthetic modifications or altered nucleotide analogues. One having ordinary skill in the art would recognize that the type of modification that may be made will depend upon the intended use of the nucleic acid molecule. For instance, when the nucleic acid molecule is used as a hybridization probe, the range of such modifications will be limited to those that permit sequence-discriminating base pairing of the resulting nucleic acid. When used to direct expression of RNA or protein *in vitro* or *in vivo*, the range of such modifications will be limited to those that permit the nucleic acid to function properly as a polymerization substrate. When the isolated nucleic acid is used as a therapeutic agent, the modifications will be limited to those that do not confer toxicity upon the isolated nucleic acid.

Accordingly, in one embodiment, a nucleic acid molecule may include nucleotide analogues that incorporate labels that are directly detectable, such as radiolabels or fluorophores, or nucleotide analogues that incorporate labels that can be visualized in a subsequent reaction, such as biotin or various haptens. The labeled nucleic acid molecules are particularly useful as hybridization probes.

Common radiolabeled analogues include those labeled with ^{33}P, ^{32}P, and ^{35}S, such as α-^{32}P-dATP, α-^{32}P-dCTP, α-^{32}P-dGTP, α-^{32}P-dTTP, α-^{32}P-3'dATP, α-^{32}P-ATP, α-^{32}P-CTP, α-^{32}P-GTP, α-^{32}P-UTP, α-^{35}S-dATP, γ-^{35}S-GTP, γ-^{33}P-dATP, and the like.

Commercially available fluorescent nucleotide analogues readily incorporated into the nucleic acids of the present invention include Cy3-dCTP, Cy3-dUTP, Cy5-dCTP, Cy3-dUTP (Amersham Biosciences, Piscataway, New Jersey, USA), fluorescein-12-dUTP, tetramethylrhodamine-6-dUTP, Texas Red®-5-dUTP, Cascade Blue®-7-dUTP, BODIPY® FL-14-dUTP, BODIPY® TMR-14-dUTP, BODIPY® TR-14-dUTP, Rhodamine Green™-5-dUTP, Oregon Green® 488-5-dUTP, Texas Red®-12-dUTP,

BODIPY® 630/650-14-dUTP, BODIPY® 650/665-14-dUTP, Alexa Fluor® 488-5-dUTP, Alexa Fluor® 532-5-dUTP, Alexa Fluor® 568-5-dUTP, Alexa Fluor® 594-5-dUTP, Alexa Fluor® 546-14-dUTP, fluorescein-12-UTP, tetramethylrhodamine-6-UTP, Texas Red®-5-UTP, Cascade Blue®-7-UTP, BODIPY® FL-14-UTP, BODIPY® TMR-14-UTP, BODIPY® TR-14-UTP, Rhodamine Green™-5-UTP, Alexa Fluor® 488-5-UTP, Alexa Fluor® 546-14-UTP (Molecular Probes, Inc. Eugene, OR, USA). One may also custom synthesize nucleotides having other fluorophores. *See* Henegariu *et al.*, *Nature Biotechnol.* 18: 345-348 (2000).

Haptens that are commonly conjugated to nucleotides for subsequent labeling include biotin (biotin-11-dUTP, Molecular Probes, Inc., Eugene, OR, USA; biotin-21-UTP, biotin-21-dUTP, Clontech Laboratories, Inc., Palo Alto, CA, USA), digoxigenin (DIG-11-dUTP, alkali labile, DIG-11-UTP, Roche Diagnostics Corp., Indianapolis, IN, USA), and dinitrophenyl (dinitrophenyl-11-dUTP, Molecular Probes, Inc., Eugene, OR, USA).

Nucleic acid molecules of the present invention can be labeled by incorporation of labeled nucleotide analogues into the nucleic acid. Such analogues can be incorporated by enzymatic polymerization, such as by nick translation, random priming, polymerase chain reaction (PCR), terminal transferase tailing, and end-filling of overhangs, for DNA molecules, and *in vitro* transcription driven, *e.g.*, from phage promoters, such as T7, T3, and SP6, for RNA molecules. Commercial kits are readily available for each such labeling approach. Analogues can also be incorporated during automated solid phase chemical synthesis. Labels can also be incorporated after nucleic acid synthesis, with the 5' phosphate and 3' hydroxyl providing convenient sites for post-synthetic covalent attachment of detectable labels.

Other post-synthetic approaches also permit internal labeling of nucleic acids. For example, fluorophores can be attached using a cisplatin reagent that reacts with the N7 of guanine residues (and, to a lesser extent, adenine bases) in DNA, RNA, and Peptide Nucleic Acids (PNA) to provide a stable coordination complex between the nucleic acid and fluorophore label (Universal Linkage System) (available from Molecular Probes, Inc., Eugene, OR, USA and Amersham Pharmacia Biotech, Piscataway, NJ, USA); *see* Alers *et al.*, *Genes, Chromosomes & Cancer* 25: 301- 305 (1999); Jelsma *et al.*, *J. NIH Res.* 5: 82 (1994); Van Belkum *et al.*, *BioTechniques* 16: 148-153 (1994). Alternatively, nucleic acids can be labeled using a disulfide-containing linker (FastTag™ Reagent, Vector

Laboratories, Inc., Burlingame, CA, USA) that is photo- or thermally coupled to the target nucleic acid using aryl azide chemistry; after reduction, a free thiol is available for coupling to a hapten, fluorophore, sugar, affinity ligand, or other marker.

One or more independent or interacting labels can be incorporated into the nucleic acid molecules of the present invention. For example, both a fluorophore and a moiety that in proximity thereto acts to quench fluorescence can be included to report specific hybridization through release of fluorescence quenching or to report exonucleotidic excision. *See, e.g.,* Tyagi *et al.*, *Nature Biotechnol.* 14: 303-308 (1996); Tyagi *et al.*, *Nature Biotechnol.* 16: 49-53 (1998); Sokol *et al.*, *Proc. Natl. Acad. Sci. USA* 95: 11538-11543 (1998); Kostrikis *et al.*, *Science* 279: 1228-1229 (1998); Marras *et al.*, *Genet. Anal.* 14: 151-156 (1999); Holland *et al.*, *Proc. Natl. Acad. Sci. USA* 88: 7276-7280 (1991); Heid *et al.*, *Genome Res.* 6(10): 986-94 (1996); Kuimelis *et al.*, *Nucleic Acids Symp. Ser.* (37): 255-6 (1997); and U.S. Patent Nos. 5,846,726, 5,925,517, 5,925,517, 5,723,591 and 5,538,848, the disclosures of which are incorporated herein by reference in their entireties.

Nucleic acid molecules of the present invention may also be modified by altering one or more native phosphodiester internucleoside bonds to more nuclease-resistant, internucleoside bonds. *See* Hartmann *et al.* (eds.), Manual of Antisense Methodology: Perspectives in Antisense Science, Kluwer Law International (1999); Stein *et al.* (eds.), Applied Antisense Oligonucleotide Technology, Wiley-Liss (1998); Chadwick *et al.* (eds.), Oligonucleotides as Therapeutic Agents – Symposium No. 209, John Wiley & Son Ltd (1997). Such altered internucleoside bonds are often desired for techniques or for targeted gene correction, Gamper *et al.*, *Nucl. Acids Res.* 28(21): 4332-4339 (2000). For double-stranded RNA inhibition which may utilize either natural ds RNA or ds RNA modified in its, sugar, phosphate or base, *see* Hannon, *Nature* 418(11): 244-251 (2002); Fire *et al.* in WO 99/32619; Tuschl *et al.* in US2002/0086356; Kruetzer *et al.* in WO 00/44895, the disclosures of which are incorporated herein by reference in their entirety. For circular antisense, see Kool in U.S. Patent No. 5,426,180, the disclosure of which is incorporated herein by reference in its entirety.

Modified oligonucleotide backbones include, without limitation, phosphorothioates, chiral phosphorothioates, phosphorodithioates, phosphotriesters, aminoalkylphosphotriesters, methyl and other alkyl phosphonates including 3'-alkylene phosphonates and chiral phosphonates, phosphinates, phosphoramidates including

3'-amino phosphoramidate and aminoalkylphosphoramidates, thionophosphoramidates, thionoalkylphosphonates, thionoalkylphosphotriesters, and boranophosphates having normal 3'-5' linkages, 2'-5' linked analogs of these, and those having inverted polarity wherein the adjacent pairs of nucleoside units are linked 3'-5' to 5'-3' or 2'-5' to 5'-2'. Representative U.S. Patents that teach the preparation of the above phosphorus-containing linkages include, but are not limited to, U.S. Patent Nos. 3,687,808; 4,469,863; 4,476,301; 5,023,243; 5,177,196; 5,188,897; 5,264,423; 5,276,019; 5,278,302; 5,286,717; 5,321,131; 5,399,676; 5,405,939; 5,453,496; 5,455,233; 5,466,677; 5,476,925; 5,519,126; 5,536,821; 5,541,306; 5,550,111; 5,563,253; 5,571,799; 5,587,361; and 5,625,050, the disclosures of which are incorporated herein by reference in their entireties. In a preferred embodiment, the modified internucleoside linkages may be used for antisense techniques.

Other modified oligonucleotide backbones do not include a phosphorus atom, but have backbones that are formed by short chain alkyl or cycloalkyl internucleoside linkages, mixed heteroatom and alkyl or cycloalkyl internucleoside linkages, or one or more short chain heteroatomic or heterocyclic internucleoside linkages. These include those having morpholino linkages (formed in part from the sugar portion of a nucleoside); siloxane backbones; sulfide, sulfoxide and sulfone backbones; formacetyl and thioformacetyl backbones; methylene formacetyl and thioformacetyl backbones; alkene containing backbones; sulfamate backbones; methyleneimino and methylenehydrazino backbones; sulfonate and sulfonamide backbones; amide backbones; and others having mixed N, O, S and CH_2 component parts. Representative U.S. patents that teach the preparation of the above backbones include, but are not limited to, U.S. Patent Nos. 5,034,506; 5,166,315; 5,185,444; 5,214,134; 5,216,141; 5,235,033; 5,264,562; 5,264,564; 5,405,938; 5,434,257; 5,466,677; 5,470,967; 5,489,677; 5,541,307; 5,561,225; 5,596,086; 5,602,240; 5,610,289; 5,602,240; 5,608,046; 5,610,289; 5,618,704; 5,623,070; 5,663,312; 5,633,360; 5,677,437 and 5,677,439; the disclosures of which are incorporated herein by reference in their entireties.

In other preferred nucleic acid molecules, both the sugar and the internucleoside linkage are replaced with novel groups, such as peptide nucleic acids (PNA). In PNA compounds, the phosphodiester backbone of the nucleic acid is replaced with an amide-containing backbone, in particular by repeating N-(2-aminoethyl) glycine units linked by amide bonds. Nucleobases are bound directly or indirectly to aza nitrogen atoms of the amide portion of the backbone, typically by methylene carbonyl linkages. PNA can be

synthesized using a modified peptide synthesis protocol. PNA oligomers can be synthesized by both Fmoc and tBoc methods. Representative U.S. patents that teach the preparation of PNA compounds include, but are not limited to, U.S. Patent Nos. 5,539,082; 5,714,331; and 5,719,262, each of which is herein incorporated by reference in its entirety. Automated PNA synthesis is readily achievable on commercial synthesizers (*see, e.g.*, "PNA User's Guide," Rev. 2, February 1998, Perseptive Biosystems Part No. 60138, Applied Biosystems, Inc., Foster City, CA). PNA molecules are advantageous for a number of reasons. First, because the PNA backbone is uncharged, PNA/DNA and PNA/RNA duplexes have a higher thermal stability than is found in DNA/DNA and DNA/RNA duplexes. The Tm of a PNA/DNA or PNA/RNA duplex is generally 1°C higher per base pair than the Tm of the corresponding DNA/DNA or DNA/RNA duplex (in 100 mM NaCl). Second, PNA molecules can also form stable PNA/DNA complexes at low ionic strength, under conditions in which DNA/DNA duplex formation does not occur. Third, PNA also demonstrates greater specificity in binding to complementary DNA because a PNA/DNA mismatch is more destabilizing than DNA/DNA mismatch. A single mismatch in mixed a PNA/DNA 15-mer lowers the Tm by 8–20°C (15°C on average). In the corresponding DNA/DNA duplexes, a single mismatch lowers the Tm by 4–16°C (11°C on average). Because PNA probes can be significantly shorter than DNA probes, their specificity is greater. Fourth, PNA oligomers are resistant to degradation by enzymes, and the lifetime of these compounds is extended both *in vivo* and *in vitro* because nucleases and proteases do not recognize the PNA polyamide backbone with nucleobase sidechains. *See, e.g.*, Ray *et al.*, *FASEB J.* 14(9): 1041-60 (2000); Nielsen *et al.*, *Pharmacol Toxicol.* 86(1): 3-7 (2000); Larsen *et al.*, *Biochim Biophys Acta.* 1489(1): 159-66 (1999); Nielsen, *Curr. Opin. Struct. Biol.* 9(3): 353-7 (1999), and Nielsen, *Curr. Opin. Biotechnol.* 10(1): 71-5 (1999).

Nucleic acid molecules may be modified compared to their native structure throughout the length of the nucleic acid molecule or can be localized to discrete portions thereof. As an example of the latter, chimeric nucleic acids can be synthesized that have discrete DNA and RNA domains and that can be used for targeted gene repair and modified PCR reactions, as further described in, Misra *et al.*, *Biochem.* 37: 1917-1925 (1998); and Finn *et al.*, *Nucl. Acids Res.* 24: 3357-3363 (1996), and U.S. Patent Nos. 5,760,012 and 5,731,181, the disclosures of which are incorporated herein by reference in their entireties.

Unless otherwise specified, nucleic acid molecules of the present invention can include any topological conformation appropriate to the desired use; the term thus explicitly comprehends, among others, single-stranded, double-stranded, triplexed, quadruplexed, partially double-stranded, partially-triplexed, partially-quadruplexed, branched, hairpinned, circular, and padlocked conformations. Padlocked conformations and their utilities are further described in Banér *et al.*, *Curr. Opin. Biotechnol.* 12: 11-15 (2001); Escude *et al.*, *Proc. Natl. Acad. Sci. USA* 14: 96(19):10603-7 (1999); and Nilsson *et al.*, *Science* 265(5181): 2085-8 (1994). Triplexed and quadruplexed conformations, and their utilities, are reviewed in Praseuth *et al.*, *Biochim. Biophys. Acta.* 1489(1): 181-206 (1999); Fox, *Curr. Med. Chem.* 7(1): 17-37 (2000); Kochetkova *et al.*, *Methods Mol. Biol.* 130: 189-201 (2000); Chan *et al.*, *J. Mol. Med.* 75(4): 267-82 (1997); Rowley *et al.*, *Mol Med* 5(10): 693-700 (1999); Kool, *Annu Rev Biophys Biomol Struct.* 25: 1-28 (1996).

SNP Polymorphisms

Commonly, sequence differences between individuals involve differences in single nucleotide positions. SNPs may account for 90% of human DNA polymorphism. Collins *et al.*, 8 *Genome Res.* 1229-31 (1998). SNPs include single base pair positions in genomic DNA at which different sequence alternatives (alleles) exist in a population. In addition, the least frequent allele generally must occur at a frequency of 1% or greater. DNA sequence variants with a reasonably high population frequency are observed approximately every 1,000 nucleotide across the genome, with estimates as high as 1 SNP per 350 base pairs. Wang *et al.*, 280 *Science* 1077-82 (1998); Harding *et al.*, 60 Am. J. Human Genet. 772-89 (1997); Taillon-Miller *et al.*, 8 *Genome Res.* 748-54 (1998); Cargill *et al.*, 22 *Nat. Genet.* 231-38 (1999); and Semple *et al.*, 16 *Bioinform. Disc. Note* 735-38 (2000). The frequency of SNPs varies with the type and location of the change. In base substitutions, two-thirds of the substitutions involve the C-T and G-A type. This variation in frequency can be related to 5-methylcytosine deamination reactions that occur frequently, particularly at CpG dinucleotides. Regarding location, SNPs occur at a much higher frequency in non-coding regions than in coding regions. Information on over one million variable sequences is already publicly available via the Internet and more such markers are available from commercial providers of genetic information. Kwok and Gu, 5 *Med. Today* 538-53 (1999).

Several definitions of SNPs exist. See, e.g., Brooks, 235 *Gene* 177-86 (1999). As used herein, the term "single nucleotide polymorphism" or "SNP" includes all single base variants, thus including nucleotide insertions and deletions in addition to single nucleotide substitutions. There are two types of nucleotide substitutions. A transition is the replacement of one purine by another purine or one pyrimidine by another pyrimidine. A transversion is the replacement of a purine for a pyrimidine, or vice versa.

Numerous methods exist for detecting SNPs within a nucleotide sequence. A review of many of these methods can be found in Landegren *et al.*, 8 *Genome Res.* 769-76 (1998). For example, a SNP in a genomic sample can be detected by preparing a Reduced Complexity Genome (RCG) from the genomic sample, then analyzing the RCG for the presence or absence of a SNP. See, e.g., WO 00/18960 which is herein incorporated by reference in its entirety. Multiple SNPs in a population of target polynucleotides in parallel can be detected using, for example, the methods of WO 00/50869 which is herein incorporated by reference in its entirety. Other SNP detection methods include the methods of U.S. Pat. Nos. 6,297,018 and 6,322,980 which are herein incorporated by reference in their entirety. Furthermore, SNPs can be detected by restriction fragment length polymorphism (RFLP) analysis. See, e.g., U.S. Pat. Nos. 5,324,631; 5,645,995 which are herein incorporated by reference in their entirety. RFLP analysis of SNPs, however, is limited to cases where the SNP either creates or destroys a restriction enzyme cleavage site. SNPs can also be detected by direct sequencing of the nucleotide sequence of interest. In addition, numerous assays based on hybridization have also been developed to detect SNPs and mismatch distinction by polymerases and ligases. Several web sites provide information about SNPs including Ensembl on the World Wide Web at ensemble.org, Sanger Institute on the World Wide Web at sanger.ac.uk/genetics/exon/, National Center for Biotechnology Information (NCBI) on the World Wide Web at ncbi.nlm.nih.gov/SNP/ , The SNP Consortium Ltd. on the World Wide Web at snp.cshl.org. The chromosomal locations for the compositions disclosed herein are provided below. In addition, one of ordinary skill in the art could use a BLAST against the genome or any of the databases cited above to find the chromosomal location. Another a preferred method to find the genomic coordinates and associated SNPs would be to use the BLAT tool (genome.ucsc.edu, Kent et al. 2001, The Human Genome Browser at UCSC, Genome Research 996-1006 or Kent 2002 BLAT —The BLAST -Like

Alignment Tool Genome Reseach, 1-9). All web sites above were accessed December 3, 2003.

RNA interference

RNA interference refers to the process of sequence-specific post transcriptional gene silencing in animals mediated by short interfering RNAs (siRNA). Fire *et al.*, 1998, *Nature*, 391, 806. The corresponding process in plants is commonly referred to as post transcriptional gene silencing or RNA silencing and is also referred to as quelling in fungi. The process of post transcriptional gene silencing is thought to be an evolutionarily conserved cellular defense mechanism used to prevent the expression of foreign genes which is commonly shared by diverse flora and phyla. Fire *et al.*, 1999, *Trends Genet.*, 15, 358. Such protection from foreign gene expression may have evolved in response to the production of double-stranded RNAs (dsRNA) derived from viral infection or the random integration of transposon elements into a host genome via a cellular response that specifically destroys homologous single-stranded RNA or viral genomic RNA. The presence of dsRNA in cells triggers the RNAi response though a mechanism that has yet to be fully characterized. This mechanism appears to be different from the interferon response that results from dsRNA mediated activation of protein kinase PKR and 2',5'-oligoadenylate synthetase resulting in non-specific cleavage of mRNA by ribonuclease L.

The presence of long dsRNAs in cells stimulates the activity of a ribonuclease III enzyme referred to as dicer. Dicer is involved in the processing of the dsRNA into short pieces of dsRNA known as short interfering RNAs (siRNA). Berstein *et al.*, 2001, *Nature*, 409, 363. Short interfering RNAs derived from dicer activity are typically about 21-23 nucleotides in length and comprise about 19 base pair duplexes. Dicer has also been implicated in the excision of 21 and 22 nucleotide small temporal RNAs (stRNA) from precursor RNA of conserved structure that are implicated in translational control. Hutvagner *et al.*, 2001, *Science*, 293, 834. The RNAi response also features an endonuclease complex containing a siRNA, commonly referred to as an RNA-induced silencing complex (RISC), which mediates cleavage of single-stranded RNA having sequence complementary to the antisense strand of the siRNA duplex. Cleavage of the target RNA takes place in the middle of the region complementary to the antisense strand of the siRNA duplex. Elbashir *et al.*, 2001, *Genes Dev.*, 15, 188.

Short interfering RNA mediated RNAi has been studied in a variety of systems. Fire *et al.*, 1998, *Nature*, 391, 806, were the first to observe RNAi in C. Elegans. Wianny and Goetz, 1999, *Nature Cell Biol.*, 2, 70, describe RNAi mediated by dsRNA in mouse embryos. Hammond *et al.*, 2000, *Nature*, 404, 293, describe RNAi in Drosophila cells transfected with dsRNA. Elbashir *et al.*, 2001, *Nature*, 411, 494, describe RNAi induced by introduction of duplexes of synthetic 21-nucleotide RNAs in cultured mammalian cells including human embryonic kidney and HeLa cells. Recent work in Drosophila embryonic lysates (Elbashir *et al.*, 2001, *EMBO J.*, 20, 6877) has revealed certain requirements for siRNA length, structure, chemical composition, and sequence that are essential to mediate efficient RNAi activity. These studies have shown that 21 nucleotide siRNA duplexes are most active when containing two nucleotide 3'-overhangs. Furthermore, complete substitution of one or both siRNA strands with 2'-deoxy (2'-H) or 2'-O-methyl nucleotides abolishes RNAi activity, whereas substitution of the 3'-terminal siRNA overhang nucleotides with deoxy nucleotides (2'-H) was shown to be tolerated. Single mismatch sequences in the center of the siRNA duplex were also shown to abolish RNAi activity. In addition, these studies also indicate that the position of the cleavage site in the target RNA is defined by the 5'-end of the siRNA guide sequence rather than the 3'-end. Elbashir et al., 2001, *EMBO J.*, 20, 6877. Other studies have indicated that a 5'-phosphate on the target-complementary strand of a siRNA duplex is required for siRNA activity and that ATP is utilized to maintain the 5'-phosphate moiety on the siRNA. Nykanen et al., 2001, *Cell*, 107, 309.

Studies have shown that replacing the 3'-overhanging segments of a 21-mer siRNA duplex having 2 nucleotide 3' overhangs with deoxyribonucleotides does not have an adverse effect on RNAi activity. Replacing up to 4 nucleotides on each end of the siRNA with deoxyribonucleotides has been reported to be well tolerated whereas complete substitution with deoxyribonucleotides results in no RNAi activity. Elbashir *et al.*, 2001, *EMBO J.*, 20, 6877. In addition, Elbashir et al., supra, also report that substitution of siRNA with 2'-O-methyl nucleotides completely abolishes RNAi activity. Li et al., WO 00/44914, and Beach et al., WO 01/68836 both suggest that siRNA "may include modifications to either the phosphate-sugar back bone or the nucleoside to include at least one of a nitrogen or sulfur heteroatom", however neither application teaches to what extent these modifications are tolerated in siRNA molecules nor provides any examples of such modified siRNA. Kreutzer and Limmer, Canadian Patent Application No. 2,359,180, also

describe certain chemical modifications for use in dsRNA constructs in order to counteract activation of double-stranded RNA-dependent protein kinase PKR, specifically 2'-amino or 2'-O-methyl nucleotides, and nucleotides containing a 2'-O or 4'-C methylene bridge. However, Kreutzer and Limmer similarly fail to show to what extent these modifications are tolerated in siRNA molecules nor do they provide any examples of such modified siRNA.

Parrish et al., 2000, *Molecular Cell*, 6, 1977-1087, tested certain chemical modifications targeting the unc-22 gene in C. elegans using long (>25 nt) siRNA transcripts. The authors describe the introduction of thiophosphate residues into these siRNA transcripts by incorporating thiophosphate nucleotide analogs with T7 and T3 RNA polymerase and observed that "RNAs with two [phosphorothioate] modified bases also had substantial decreases in effectiveness as RNAi triggers; [phosphorothioate] modification of more than two residues greatly destabilized the RNAs in vitro and we were not able to assay interference activities." Parrish et al. at 1081. The authors also tested certain modifications at the 2'-position of the nucleotide sugar in the long siRNA transcripts and observed that substituting deoxynucleotides for ribonucleotides "produced a substantial decrease in interference activity", especially in the case of Uridine to Thymidine and/or Cytidine to deoxy-Cytidine substitutions. Parrish et al. In addition, the authors tested certain base modifications, including substituting 4-thiouracil, 5-bromouracil, 5-iodouracil, 3-(aminoallyl)uracil for uracil, and inosine for guanosine in sense and antisense strands of the siRNA, and found that whereas 4-thiouracil and 5-bromouracil were all well tolerated, inosine "produced a substantial decrease in interference activity" when incorporated in either strand. Incorporation of 5-iodouracil and 3-(aminoallyl)uracil in the antisense strand resulted in substantial decrease in RNAi activity as well.

Beach et al., WO 01/68836, describes specific methods for attenuating gene expression using endogenously derived dsRNA. Tuschl et al., WO 01/75164, describes a Drosophila in vitro RNAi system and the use of specific siRNA molecules for certain functional genomic and certain therapeutic applications; although Tuschl, 2001, *Chem. Biochem.*, 2, 239-245, doubts that RNAi can be used to cure genetic diseases or viral infection due "to the danger of activating interferon response". Li et al., WO 00/44914, describes the use of specific dsRNAs for use in attenuating the expression of certain target

genes. Zernicka-Goetz et al., WO 01/36646, describes certain methods for inhibiting the expression of particular genes in mammalian cells using certain dsRNA molecules. Fire et al., WO 99/32619, U.S. Patent No. 6,506,559, the contents of which are hereby incorporated by reference in their entirety, describes particular methods for introducing certain dsRNA molecules into cells for use in inhibiting gene expression. Plaetinck et al., WO 00/01846, describes certain methods for identifying specific genes responsible for conferring a particular phenotype in a cell using specific dsRNA molecules. Mello et al., WO 01/29058, describes the identification of specific genes involved in dsRNA mediated RNAi. Deschamps Depaillette et al., International PCT Publication No. WO 99/07409, describes specific compositions consisting of particular dsRNA molecules combined with certain anti-viral agents. Driscoll et al., International PCT Publication No. WO 01/49844, describes specific DNA constructs for use in facilitating gene silencing in targeted organisms. Parrish et al., 2000, Molecular Cell, 6, 1977-1087, describes specific chemically modified siRNA constructs targeting the unc-22 gene of C. elegans. Tuschl et al., International PCT Publication No. WO 02/44321, describe certain synthetic siRNA constructs.

Methods for Using Nucleic Acid Molecules as Probes and Primers

The isolated nucleic acid molecules of the present invention can be used as hybridization probes to detect, characterize, and quantify hybridizing nucleic acids in, and isolate hybridizing nucleic acids from, both genomic and transcript-derived nucleic acid samples. When free in solution, such probes are typically, but not invariably, detectably labeled; bound to a substrate, as in a microarray, such probes are typically, but not invariably unlabeled.

In one embodiment, the isolated nucleic acid molecules of the present invention can be used as probes to detect and characterize gross alterations in the gene of an OSNA, such as deletions, insertions, translocations, and duplications of the OSNA genomic locus through fluorescence *in situ* hybridization (FISH) to chromosome spreads. *See, e.g.*, Andreeff *et al.* (eds.), Introduction to Fluorescence *In Situ* Hybridization: Principles and Clinical Applications, John Wiley & Sons (1999). The isolated nucleic acid molecules of the present invention can be used as probes to assess smaller genomic alterations using, *e.g.*, Southern blot detection of restriction fragment length polymorphisms. The isolated nucleic acid molecules of the present invention can be used as probes to isolate genomic

clones that include a nucleic acid molecule of the present invention, which thereafter can be restriction mapped and sequenced to identify deletions, insertions, translocations, and substitutions (single nucleotide polymorphisms, SNPs) at the sequence level. Alternatively, detection techniques such as molecular beacons may be used, see Kostrikis *et al. Science* 279:1228-1229 (1998).

The isolated nucleic acid molecules of the present invention can also be used as probes to detect, characterize, and quantify OSNA in, and isolate OSNA from, transcript-derived nucleic acid samples. In one embodiment, the isolated nucleic acid molecules of the present invention can be used as hybridization probes to detect, characterize by length, and quantify mRNA by Northern blot of total or poly-A^+- selected RNA samples. In another embodiment, the isolated nucleic acid molecules of the present invention can be used as hybridization probes to detect, characterize by location, and quantify mRNA by *in situ* hybridization to tissue sections. *See*, *e.g.*, Schwarchzacher *et al.*, In Situ Hybridization, Springer-Verlag New York (2000). In another preferred embodiment, the isolated nucleic acid molecules of the present invention can be used as hybridization probes to measure the representation of clones in a cDNA library or to isolate hybridizing nucleic acid molecules acids from cDNA libraries, permitting sequence level characterization of mRNAs that hybridize to OSNAs, including, without limitations, identification of deletions, insertions, substitutions, truncations, alternatively spliced forms and single nucleotide polymorphisms. In yet another preferred embodiment, the nucleic acid molecules of the instant invention may be used in microarrays.

All of the aforementioned probe techniques are well within the skill in the art, and are described at greater length in standard texts such as Sambrook (2001), *supra*; Ausubel (1999), *supra*; and Walker *et al.* (eds.), The Nucleic Acids Protocols Handbook, Humana Press (2000).

In another embodiment, a nucleic acid molecule of the invention may be used as a probe or primer to identify and/or amplify a second nucleic acid molecule that selectively hybridizes to the nucleic acid molecule of the invention. In this embodiment, it is preferred that the probe or primer be derived from a nucleic acid molecule encoding an OSP. More preferably, the probe or primer is derived from a nucleic acid molecule encoding a polypeptide having an amino acid sequence of SEQ ID NO: 129-295. Also preferred are probes or primers derived from an OSNA. More preferred are probes or

primers derived from a nucleic acid molecule having a nucleotide sequence of SEQ ID NO: 1-128.

In general, a probe or primer is at least 10 nucleotides in length, more preferably at least 12, more preferably at least 14 and even more preferably at least 16 or 17 nucleotides in length. In an even more preferred embodiment, the probe or primer is at least 18 nucleotides in length, even more preferably at least 20 nucleotides and even more preferably at least 22 nucleotides in length. Primers and probes may also be longer in length. For instance, a probe or primer may be 25 nucleotides in length, or may be 30, 40 or 50 nucleotides in length. Methods of performing nucleic acid hybridization using oligonucleotide probes are well known in the art. *See, e.g.*, Sambrook *et al.*, 1989, *supra*, Chapter 11 and pp. 11.31-11.32 and 11.40-11.44, which describes radiolabeling of short probes, and pp. 11.45-11.53, which describe hybridization conditions for oligonucleotide probes, including specific conditions for probe hybridization (pp. 11.50-11.51).

Methods of performing primer-directed amplification are also well known in the art. Methods for performing the polymerase chain reaction (PCR) are compiled, *inter alia*, in McPherson, PCR Basics: From Background to Bench, Springer Verlag (2000); Innis *et al.* (eds.), PCR Applications: Protocols for Functional Genomics, Academic Press (1999); Gelfand *et al.* (eds.), PCR Strategies, Academic Press (1998); Newton *et al.*, PCR, Springer-Verlag New York (1997); Burke (ed.), PCR: Essential Techniques, John Wiley & Son Ltd (1996); White (ed.), PCR Cloning Protocols: From Molecular Cloning to Genetic Engineering, Vol. 67, Humana Press (1996); and McPherson *et al.* (eds.), PCR 2: A Practical Approach, Oxford University Press, Inc. (1995). Methods for performing RT-PCR are collected, *e.g.*, in Siebert *et al.* (eds.), Gene Cloning and Analysis by RT-PCR, Eaton Publishing Company/Bio Techniques Books Division, 1998; and Siebert (ed.), PCR Technique:RT-PCR, Eaton Publishing Company/ BioTechniques Books (1995).

PCR and hybridization methods may be used to identify and/or isolate nucleic acid molecules of the present invention including allelic variants, homologous nucleic acid molecules and fragments. PCR and hybridization methods may also be used to identify, amplify and/or isolate nucleic acid molecules of the present invention that encode homologous proteins, analogs, fusion proteins or muteins of the invention. Nucleic acid primers as described herein can be used to prime amplification of nucleic acid molecules of the invention, using transcript-derived or genomic DNA as the template.

These nucleic acid primers can also be used, for example, to prime single base extension (SBE) for SNP detection (*See, e.g.*, U.S. Pat. No. 6,004,744, the disclosure of which is incorporated herein by reference in its entirety).

Isothermal amplification approaches, such as rolling circle amplification, are also now well-described. *See, e.g.*, Schweitzer *et al.*, *Curr. Opin. Biotechnol.* 12(1): 21-7 (2001); International Patent publications WO 97/19193 and WO 00/15779, and U.S. Patent Nos. 5,854,033 and 5,714,320, the disclosures of which are incorporated herein by reference in their entireties. Rolling circle amplification can be combined with other techniques to facilitate SNP detection. *See, e.g.*, Lizardi *et al.*, *Nature Genet.* 19(3): 225-32 (1998).

Nucleic acid molecules of the present invention may be bound to a substrate either covalently or noncovalently. The substrate can be porous or solid, planar or non-planar, unitary or distributed. The bound nucleic acid molecules may be used as hybridization probes, and may be labeled or unlabeled. In a preferred embodiment, the bound nucleic acid molecules are unlabeled.

In one embodiment, the nucleic acid molecule of the present invention is bound to a porous substrate, *e.g.*, a membrane, typically comprising nitrocellulose, nylon, or positively charged derivatized nylon. The nucleic acid molecule of the present invention can be used to detect a hybridizing nucleic acid molecule that is present within a labeled nucleic acid sample, *e.g.*, a sample of transcript-derived nucleic acids. In another embodiment, the nucleic acid molecule is bound to a solid substrate, including, without limitation, glass, amorphous silicon, crystalline silicon or plastics. Examples of plastics include, without limitation, polymethylacrylic, polyethylene, polypropylene, polyacrylate, polymethylmethacrylate, polyvinylchloride, polytetrafluoroethylene, polystyrene, polycarbonate, polyacetal, polysulfone, celluloseacetate, cellulosenitrate, nitrocellulose, or mixtures thereof. The solid substrate may be any shape, including rectangular, disk-like and spherical. In a preferred embodiment, the solid substrate is a microscope slide or slide-shaped substrate.

The nucleic acid molecule of the present invention can be attached covalently to a surface of the support substrate or applied to a derivatized surface in a chaotropic agent that facilitates denaturation and adherence by presumed noncovalent interactions, or some combination thereof. The nucleic acid molecule of the present invention can be bound to a substrate to which a plurality of other nucleic acids are concurrently bound, hybridization

to each of the plurality of bound nucleic acids being separately detectable. At low density, *e.g.* on a porous membrane, these substrate-bound collections are typically denominated macroarrays; at higher density, typically on a solid support, such as glass, these substrate bound collections of plural nucleic acids are colloquially termed microarrays. As used herein, the term microarray includes arrays of all densities. It is, therefore, another aspect of the invention to provide microarrays that comprise one or more of the nucleic acid molecules of the present invention.

In yet another embodiment, the invention is directed to single exon probes based on the OSNAs disclosed herein.

Expression Vectors, Host Cells and Recombinant Methods of Producing Polypeptides

Another aspect of the present invention provides vectors that comprise one or more of the isolated nucleic acid molecules of the present invention, and host cells in which such vectors have been introduced.

The vectors can be used, *inter alia*, for propagating the nucleic acid molecules of the present invention in host cells (cloning vectors), for shuttling the nucleic acid molecules of the present invention between host cells derived from disparate organisms (shuttle vectors), for inserting the nucleic acid molecules of the present invention into host cell chromosomes (insertion vectors), for expressing sense or antisense RNA transcripts of the nucleic acid molecules of the present invention *in vitro* or within a host cell, and for expressing polypeptides encoded by the nucleic acid molecules of the present invention, alone or as fusion proteins with heterologous polypeptides (expression vectors). Vectors are by now well known in the art, and are described, *inter alia*, in Jones *et al.* (eds.), Vectors: Cloning Applications: Essential Techniques (Essential Techniques Series), John Wiley & Son Ltd. (1998); Jones *et al.* (eds.), Vectors: Expression Systems: Essential Techniques (Essential Techniques Series), John Wiley & Son Ltd. (1998); Gacesa *et al.*, Vectors: Essential Data, John Wiley & Sons Ltd. (1995); Cid-Arregui (eds.), Viral Vectors: Basic Science and Gene Therapy, Eaton Publishing Co. (2000); Sambrook (2001), *supra*; Ausubel (1999), *supra*. Furthermore, a variety of vectors are available commercially. Use of existing vectors and modifications thereof are well within the skill in the art. Thus, only basic features need be described here.

Nucleic acid sequences may be expressed by operatively linking them to an expression control sequence in an appropriate expression vector and employing that expression vector to transform an appropriate unicellular host. Expression control sequences are sequences that control the transcription, post-transcriptional events and translation of nucleic acid sequences. Such operative linking of a nucleic acid sequence of this invention to an expression control sequence, of course, includes, if not already part of the nucleic acid sequence, the provision of a translation initiation codon, ATG or GTG, in the correct reading frame upstream of the nucleic acid sequence.

A wide variety of host/expression vector combinations may be employed in expressing the nucleic acid sequences of this invention. Useful expression vectors, for example, may consist of segments of chromosomal, non-chromosomal and synthetic nucleic acid sequences.

In one embodiment, prokaryotic cells may be used with an appropriate vector. Prokaryotic host cells are often used for cloning and expression. In a preferred embodiment, prokaryotic host cells include *E. coli*, *Pseudomonas*, *Bacillus* and *Streptomyces*. In a preferred embodiment, bacterial host cells are used to express the nucleic acid molecules of the instant invention. Useful expression vectors for bacterial hosts include bacterial plasmids, such as those from *E. coli*, *Bacillus* or *Streptomyces*, including pBluescript, pGEX-2T, pUC vectors, col E1, pCR1, pBR322, pMB9 and their derivatives, wider host range plasmids, such as RP4, phage DNAs, *e.g.*, the numerous derivatives of phage lambda, *e.g.*, NM989, λGT10 and λGT11, and other phages, *e.g.*, M13 and filamentous single-stranded phage DNA. Where *E. coli* is used as host, selectable markers are, analogously, chosen for selectivity in gram negative bacteria: *e.g.*, typical markers confer resistance to antibiotics, such as ampicillin, tetracycline, chloramphenicol, kanamycin, streptomycin and zeocin; auxotrophic markers can also be used.

In other embodiments, eukaryotic host cells, such as yeast, insect, mammalian or plant cells, may be used. Yeast cells, typically *S. cerevisiae*, are useful for eukaryotic genetic studies, due to the ease of targeting genetic changes by homologous recombination and the ability to easily complement genetic defects using recombinantly expressed proteins. Yeast cells are useful for identifying interacting protein components, *e.g.* through use of a two-hybrid system. In a preferred embodiment, yeast cells are useful for protein expression. Vectors of the present invention for use in yeast will typically, but not

invariably, contain an origin of replication suitable for use in yeast and a selectable marker that is functional in yeast. Yeast vectors include Yeast Integrating plasmids (*e.g.*, YIp5) and Yeast Replicating plasmids (the YRp and YEp series plasmids), Yeast Centromere plasmids (the YCp series plasmids), Yeast Artificial Chromosomes (YACs) which are based on yeast linear plasmids, denoted YLp, pGPD-2, 2μ plasmids and derivatives thereof, and improved shuttle vectors such as those described in Gietz *et al.*, *Gene*, 74: 527-34 (1988) (YIplac, YEplac and YCplac). Selectable markers in yeast vectors include a variety of auxotrophic markers, the most common of which are (in *Saccharomyces cerevisiae*) URA3, HIS3, LEU2, TRP1 and LYS2, which complement specific auxotrophic mutations, such as ura3-52, his3-D1, leu2-D1, trp1-D1 and lys2-201.

Insect cells may be chosen for high efficiency protein expression. Where the host cells are from *Spodoptera frugiperda, e.g.*, Sf9 and Sf21 cell lines, and expresSF™ cells (Protein Sciences Corp., Meriden, CT, USA), the vector replicative strategy is typically based upon the baculovirus life cycle. Typically, baculovirus transfer vectors are used to replace the wild-type AcMNPV polyhedrin gene with a heterologous gene of interest. Sequences that flank the polyhedrin gene in the wild-type genome are positioned 5' and 3' of the expression cassette on the transfer vectors. Following co-transfection with AcMNPV DNA, a homologous recombination event occurs between these sequences resulting in a recombinant virus carrying the gene of interest and the polyhedrin or p10 promoter. Selection can be based upon visual screening for lacZ fusion activity.

The host cells may also be mammalian cells, which are particularly useful for expression of proteins intended as pharmaceutical agents, and for screening of potential agonists and antagonists of a protein or a physiological pathway. Mammalian vectors intended for autonomous extrachromosomal replication will typically include a viral origin, such as the SV40 origin (for replication in cell lines expressing the large T-antigen, such as COS1 and COS7 cells), the papillomavirus origin, or the EBV origin for long term episomal replication (for use, *e.g.*, in 293-EBNA cells, which constitutively express the EBV EBNA-1 gene product and adenovirus E1A). Vectors intended for integration, and thus replication as part of the mammalian chromosome, can, but need not, include an origin of replication functional in mammalian cells, such as the SV40 origin. Vectors based upon viruses, such as adenovirus, adeno-associated virus, vaccinia virus, and various mammalian retroviruses, will typically replicate according to the viral replicative strategy. Selectable markers for use in mammalian cells include, but are not limited to,

resistance to neomycin (G418), blasticidin, hygromycin and zeocin, and selection based upon the purine salvage pathway using HAT medium.

Expression in mammalian cells can be achieved using a variety of plasmids, including pSV2, pBC12BI, and p91023, as well as lytic virus vectors (*e.g.*, vaccinia virus, adeno virus, and baculovirus), episomal virus vectors (*e.g.*, bovine papillomavirus), and retroviral vectors (*e.g.*, murine retroviruses). Useful vectors for insect cells include baculoviral vectors and pVL 941.

Plant cells can also be used for expression, with the vector replicon typically derived from a plant virus (*e.g.*, cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) and selectable markers chosen for suitability in plants.

It is known that codon usage of different host cells may be different. For example, a plant cell and a human cell may exhibit a difference in codon preference for encoding a particular amino acid. As a result, human mRNA may not be efficiently translated in a plant, bacteria or insect host cell. Therefore, another embodiment of this invention is directed to codon optimization. The codons of the nucleic acid molecules of the invention may be modified to resemble, as much as possible, genes naturally contained within the host cell without altering the amino acid sequence encoded by the nucleic acid molecule.

Any of a wide variety of expression control sequences may be used in these vectors to express the nucleic acid molecules of this invention. Such useful expression control sequences include the expression control sequences associated with structural genes of the foregoing expression vectors. Expression control sequences that control transcription include, *e.g.*, promoters, enhancers and transcription termination sites. Expression control sequences in eukaryotic cells that control post-transcriptional events include splice donor and acceptor sites and sequences that modify the half-life of the transcribed RNA, *e.g.*, sequences that direct poly(A) addition or binding sites for RNA-binding proteins. Expression control sequences that control translation include ribosome binding sites, sequences which direct targeted expression of the polypeptide to or within particular cellular compartments, and sequences in the 5' and 3' untranslated regions that modify the rate or efficiency of translation.

Examples of useful expression control sequences for a prokaryote, *e.g.*, *E. coli*, will include a promoter, often a phage promoter, such as phage lambda pL promoter, the trc promoter, a hybrid derived from the trp and lac promoters, the bacteriophage T7 promoter (in *E. coli* cells engineered to express the T7 polymerase), the <u>TAC</u> or <u>TRC</u>

system, the major operator and promoter regions of phage lambda, the control regions of fd coat protein, and the araBAD operon. Prokaryotic expression vectors may further include transcription terminators, such as the aspA terminator, and elements that facilitate translation, such as a consensus ribosome binding site and translation termination codon, Schomer *et al.*, *Proc. Natl. Acad. Sci. USA* 83: 8506-8510 (1986).

Expression control sequences for yeast cells, typically *S. cerevisiae*, will include a yeast promoter, such as the CYC1 promoter, the GAL1 promoter, the GAL10 promoter, ADH1 promoter, the promoters of the yeast $\underline{\alpha}$-mating system, or the GPD promoter, and will typically have elements that facilitate transcription termination, such as the transcription termination signals from the CYC1 or ADH1 gene.

Expression vectors useful for expressing proteins in mammalian cells will include a promoter active in mammalian cells. These promoters include, but are not limited to, those derived from mammalian viruses, such as the enhancer-promoter sequences from the immediate early gene of the human cytomegalovirus (CMV), the enhancer-promoter sequences from the Rous sarcoma virus long terminal repeat (RSV LTR), the enhancer-promoter from SV40 and the early and late promoters of adenovirus. Other expression control sequences include the promoter for 3-phosphoglycerate kinase or other glycolytic enzymes, the promoters of acid phosphatase. Other expression control sequences include those from the gene comprising the OSNA of interest. Often, expression is enhanced by incorporation of polyadenylation sites, such as the late SV40 polyadenylation site and the polyadenylation signal and transcription termination sequences from the bovine growth hormone (BGH) gene, and ribosome binding sites. Furthermore, vectors can include introns, such as intron II of rabbit β-globin gene and the SV40 splice elements.

Preferred nucleic acid vectors also include a selectable or amplifiable marker gene and means for amplifying the copy number of the gene of interest. Such marker genes are well known in the art. Nucleic acid vectors may also comprise stabilizing sequences (*e.g.*, ori- or ARS-like sequences and telomere-like sequences), or may alternatively be designed to favor directed or non-directed integration into the host cell genome. In a preferred embodiment, nucleic acid sequences of this invention are inserted in frame into an expression vector that allows a high level expression of an RNA which encodes a protein comprising the encoded nucleic acid sequence of interest. Nucleic acid cloning and sequencing methods are well known to those of skill in the art and are described in an assortment of laboratory manuals, including Sambrook (1989), *supra*, Sambrook (2000),

supra; Ausubel (1992), *supra;* and Ausubel (1999), *supra*. Product information from manufacturers of biological, chemical and immunological reagents also provide useful information.

Expression vectors may be either constitutive or inducible. Inducible vectors include either naturally inducible promoters, such as the trc promoter, which is regulated by the lac operon, and the pL promoter, which is regulated by tryptophan, the MMTV-LTR promoter, which is inducible by dexamethasone, or can contain synthetic promoters and/or additional elements that confer inducible control on adjacent promoters. Examples of inducible synthetic promoters are the hybrid Plac/ara-1 promoter and the PLtetO-1 promoter. The PLtetO-1 promoter takes advantage of the high expression levels from the PL promoter of phage lambda, but replaces the lambda repressor sites with two copies of operator 2 of the Tn10 tetracycline resistance operon, causing this promoter to be tightly repressed by the Tet repressor protein and induced in response to tetracycline (Tc) and Tc derivatives such as anhydrotetracycline. Vectors may also be inducible because they contain hormone response elements, such as the glucocorticoid response element (GRE) and the estrogen response element (ERE), which can confer hormone inducibility where vectors are used for expression in cells having the respective hormone receptors. To reduce background levels of expression, elements responsive to ecdysone, an insect hormone, can be used instead, with coexpression of the ecdysone receptor.

In one embodiment of the invention, expression vectors can be designed to fuse the expressed polypeptide to small protein tags that facilitate purification and/or visualization. Such tags include a polyhistidine tag that facilitates purification of the fusion protein by immobilized metal affinity chromatography, for example using NiNTA resin (Qiagen Inc., Valencia, CA, USA) or TALON™ resin (cobalt immobilized affinity chromatography medium, Clontech Labs, Palo Alto, CA, USA). The fusion protein can include a chitin-binding tag and self-excising intein, permitting chitin-based purification with self-removal of the fused tag (IMPACT™ system, New England Biolabs, Inc., Beverley, MA, USA). Alternatively, the fusion protein can include a calmodulin-binding peptide tag, permitting purification by calmodulin affinity resin (Stratagene, La Jolla, CA, USA), or a specifically excisable fragment of the biotin carboxylase carrier protein, permitting purification of *in vivo* biotinylated protein using an avidin resin and subsequent tag removal (Promega, Madison, WI, USA). As another useful alternative, the polypeptides of the present invention can be expressed as a fusion to glutathione-S-transferase, the affinity and

specificity of binding to glutathione permitting purification using glutathione affinity resins, such as Glutathione-Superflow Resin (Clontech Laboratories, Palo Alto, CA, USA), with subsequent elution with free glutathione. Other tags include, for example, the Xpress epitope, detectable by anti-Xpress antibody (Invitrogen, Carlsbad, CA, USA), a myc tag, detectable by anti-myc tag antibody, the V5 epitope, detectable by anti-V5 antibody (Invitrogen, Carlsbad, CA, USA), FLAG® epitope, detectable by anti-FLAG® antibody (Stratagene, La Jolla, CA, USA), and the HA epitope, detectable by anti-HA antibody.

For secretion of expressed polypeptides, vectors can include appropriate sequences that encode secretion signals, such as leader peptides. For example, the pSecTag2 vectors (Invitrogen, Carlsbad, CA, USA) are 5.2 kb mammalian expression vectors that carry the secretion signal from the V-J2-C region of the mouse Ig kappa-chain for efficient secretion of recombinant proteins from a variety of mammalian cell lines.

Expression vectors can also be designed to fuse proteins encoded by the heterologous nucleic acid insert to polypeptides that are larger than purification and/or identification tags. Useful protein fusions include those that permit display of the encoded protein on the surface of a phage or cell, fusions to intrinsically fluorescent proteins, such as those that have a green fluorescent protein (GFP)-like chromophore, fusions to the IgG Fc region, and fusions for use in two hybrid systems.

Vectors for phage display fuse the encoded polypeptide to, *e.g.*, the gene III protein (pIII) or gene VIII protein (pVIII) for display on the surface of filamentous phage, such as M13. *See* Barbas *et al.*, <u>Phage Display: A Laboratory Manual</u>, Cold Spring Harbor Laboratory Press (2001); Kay *et al.* (eds.), <u>Phage Display of Peptides and Proteins: A Laboratory Manual</u>, Academic Press, Inc., (1996); Abelson *et al.* (eds.), <u>Combinatorial Chemistry</u> (Methods in Enzymology, Vol. 267) Academic Press (1996). Vectors for yeast display, *e.g.* the pYD1 yeast display vector (Invitrogen, Carlsbad, CA, USA), use the α-agglutinin yeast adhesion receptor to display recombinant protein on the surface of *S. cerevisiae*. Vectors for mammalian display, *e.g.*, the pDisplay™ vector (Invitrogen, Carlsbad, CA, USA), target recombinant proteins using an N-terminal cell surface targeting signal and a C-terminal transmembrane anchoring domain of platelet derived growth factor receptor.

A wide variety of vectors now exist that fuse proteins encoded by heterologous nucleic acids to the chromophore of the substrate-independent, intrinsically fluorescent

green fluorescent protein from *Aequorea victoria* ("GFP") and its variants. The GFP-like chromophore can be selected from GFP-like chromophores found in naturally occurring proteins, such as *A. victoria* GFP (GenBank accession number AAA27721), *Renilla reniformis* GFP, FP583 (GenBank accession no. AF168419) (DsRed), FP593 (AF272711), FP483 (AF168420), FP484 (AF168424), FP595 (AF246709), FP486 (AF168421), FP538 (AF168423), and FP506 (AF168422), and need include only so much of the native protein as is needed to retain the chromophore's intrinsic fluorescence. Methods for determining the minimal domain required for fluorescence are known in the art. *See* Li *et al.*, *J. Biol. Chem.* 272: 28545-28549 (1997). Alternatively, the GFP-like chromophore can be selected from GFP-like chromophores modified from those found in nature. The methods for engineering such modified GFP-like chromophores and testing them for fluorescence activity, both alone and as part of protein fusions, are well known in the art. *See* Heim *et al.*, *Curr. Biol.* 6: 178-182 (1996) and Palm *et al.*, *Methods Enzymol.* 302: 378-394 (1999). A variety of such modified chromophores are now commercially available and can readily be used in the fusion proteins of the present invention. These include EGFP ("enhanced GFP"), EBFP ("enhanced blue fluorescent protein"), BFP2, EYFP ("enhanced yellow fluorescent protein"), ECFP ("enhanced cyan fluorescent protein") or Citrine. EGFP (*see, e.g,* Cormack *et al.*, *Gene* 173: 33–38 (1996); U.S. Patent Nos. 6,090,919 and 5,804,387, the disclosures of which are incorporated herein by reference in their entireties) is found on a variety of vectors, both plasmid and viral, which are available commercially (Clontech Labs, Palo Alto, CA, USA); EBFP is optimized for expression in mammalian cells whereas BFP2, which retains the original jellyfish codons, can be expressed in bacteria (*see, e.g,.* Heim *et al.*, *Curr. Biol.* 6: 178-182 (1996) and Cormack *et al.*, *Gene* 173: 33-38 (1996)). Vectors containing these blue-shifted variants are available from Clontech Labs (Palo Alto, CA, USA). Vectors containing EYFP, ECFP (*see, e.g.*, Heim *et al.*, *Curr. Biol.* 6: 178-182 (1996); Miyawaki *et al.*, *Nature* 388: 882-887 (1997)) and Citrine (*see, e.g.*, Heikal *et al.*, *Proc. Natl. Acad. Sci. USA* 97: 11996-12001 (2000)) are also available from Clontech Labs. The GFP-like chromophore can also be drawn from other modified GFPs, including those described in U.S. Patent Nos. 6,124,128; 6,096,865; 6,090,919; 6,066,476; 6,054,321; 6,027,881; 5,968,750; 5,874,304; 5,804,387; 5,777,079; 5,741,668; and 5,625,048, the disclosures of which are incorporated herein by reference in their entireties. *See* also Conn (ed.), Green Fluorescent Protein (Methods in Enzymology, Vol. 302), Academic Press, Inc. (1999); Yang, *et al.*, *J Biol Chem*, 273: 8212-6 (1998);

Bevis *et al.*, *Nature Biotechnology*, 20:83-7 (2002). The GFP-like chromophore of each of these GFP variants can usefully be included in the fusion proteins of the present invention.

Fusions to the IgG Fc region increase serum half-life of protein pharmaceutical products through interaction with the FcRn receptor (also denominated the FcRp receptor and the Brambell receptor, FcRb), further described in International Patent Application Nos. WO 97/43316, WO 97/34631, WO 96/32478, and WO 96/18412, the disclosures of which are incorporated herein by reference in their entireties.

For long-term, high-yield recombinant production of the polypeptides of the present invention, stable expression is preferred. Stable expression is readily achieved by integration into the host cell genome of vectors having selectable markers, followed by selection of these integrants. Vectors such as pUB6/V5-His A, B, and C (Invitrogen, Carlsbad, CA, USA) are designed for high-level stable expression of heterologous proteins in a wide range of mammalian tissue types and cell lines. pUB6/V5-His uses the promoter/enhancer sequence from the human ubiquitin C gene to drive expression of recombinant proteins: expression levels in 293, CHO, and NIH3T3 cells are comparable to levels from the CMV and human EF-1a promoters. The bsd gene permits rapid selection of stably transfected mammalian cells with the potent antibiotic blasticidin.

Replication incompetent retroviral vectors, typically derived from Moloney murine leukemia virus, also are useful for creating stable transfectants having integrated provirus. The highly efficient transduction machinery of retroviruses, coupled with the availability of a variety of packaging cell lines such as RetroPack™ PT 67, EcoPack2™-293, AmphoPack-293, and GP2-293 cell lines (all available from Clontech Laboratories, Palo Alto, CA, USA) allow a wide host range to be infected with high efficiency; varying the multiplicity of infection readily adjusts the copy number of the integrated provirus.

Of course, not all vectors and expression control sequences will function equally well to express the nucleic acid molecules of this invention. Neither will all hosts function equally well with the same expression system. However, one of skill in the art may make a selection among these vectors, expression control sequences and hosts without undue experimentation and without departing from the scope of this invention. For example, in selecting a vector, the host must be considered because the vector must be replicated in it. The vector's copy number, the ability to control that copy number, the ability to control integration, if any, and the expression of any other proteins encoded by the vector, such as

an antibiotic or other selection marker, should also be considered. The present invention further includes host cells comprising the vectors of the present invention, either present episomally within the cell or integrated, in whole or in part, into the host cell chromosome. Among other considerations, some of which are described above, a host cell strain may be chosen for its ability to process the expressed polypeptide in the desired fashion. Such post-translational modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation, and acylation, and it is an aspect of the present invention to provide OSPs with such post-translational modifications.

In selecting an expression control sequence, a variety of factors should also be considered. These include, for example, the relative strength of the sequence, its controllability, and its compatibility with the nucleic acid molecules of this invention, particularly with regard to potential secondary structures. Unicellular hosts should be selected by consideration of their compatibility with the chosen vector, the toxicity of the product coded for by the nucleic acid sequences of this invention, their secretion characteristics, their ability to fold the polypeptide correctly, their fermentation or culture requirements, and the ease of purification from them of the products coded for by the nucleic acid molecules of this invention.

The recombinant nucleic acid molecules and more particularly, the expression vectors of this invention may be used to express the polypeptides of this invention as recombinant polypeptides in a heterologous host cell. The polypeptides of this invention may be full-length or less than full-length polypeptide fragments recombinantly expressed from the nucleic acid molecules according to this invention. Such polypeptides include analogs, derivatives and muteins that may or may not have biological activity.

Vectors of the present invention will also often include elements that permit *in vitro* transcription of RNA from the inserted heterologous nucleic acid. Such vectors typically include a phage promoter, such as that from T7, T3, or SP6, flanking the nucleic acid insert. Often two different such promoters flank the inserted nucleic acid, permitting separate *in vitro* production of both sense and antisense strands.

Transformation and other methods of introducing nucleic acids into a host cell (*e.g.*, conjugation, protoplast transformation or fusion, transfection, electroporation, liposome delivery, membrane fusion techniques, high velocity DNA-coated pellets, viral infection and protoplast fusion) can be accomplished by a variety of methods which are

well known in the art (*See*, for instance, Ausubel, *supra*, and Sambrook *et al.*, *supra*). Bacterial, yeast, plant or mammalian cells are transformed or transfected with an expression vector, such as a plasmid, a cosmid, or the like, wherein the expression vector comprises the nucleic acid of interest. Alternatively, the cells may be infected by a viral expression vector comprising the nucleic acid of interest. Depending upon the host cell, vector, and method of transformation used, transient or stable expression of the polypeptide will be constitutive or inducible. One having ordinary skill in the art will be able to decide whether to express a polypeptide transiently or stably, and whether to express the protein constitutively or inducibly.

A wide variety of unicellular host cells are useful in expressing the DNA sequences of this invention. These hosts may include well known eukaryotic and prokaryotic hosts, such as strains of, fungi, yeast, insect cells such as *Spodoptera frugiperda* (SF9), animal cells such as CHO, as well as plant cells in tissue culture. Representative examples of appropriate host cells include, but are not limited to, bacterial cells, such as *E. coli*, *Caulobacter crescentus*, *Streptomyces* species, and *Salmonella typhimurium*; yeast cells, such as *Saccharomyces cerevisiae, Schizosaccharomyces pombe, Pichia pastoris*, *Pichia methanolica*; insect cell lines, such as those from *Spodoptera frugiperda, e.g.*, Sf9 and Sf21 cell lines, and expresSF™ cells (Protein Sciences Corp., Meriden, CT, USA), *Drosophila* S2 cells, and *Trichoplusia ni* High Five® Cells (Invitrogen, Carlsbad, CA, USA); and mammalian cells. Typical mammalian cells include BHK cells, BSC 1 cells, BSC 40 cells, BMT 10 cells, VERO cells, COS1 cells, COS7 cells, Chinese hamster ovary (CHO) cells, 3T3 cells, NIH 3T3 cells, 293 cells, HEPG2 cells, HeLa cells, L cells, MDCK cells, HEK293 cells, WI38 cells, murine ES cell lines (*e.g.*, from strains 129/SV, C57/BL6, DBA-1, 129/SVJ), K562 cells, Jurkat cells, and BW5147 cells. Other mammalian cell lines are well known and readily available from the American Type Culture Collection (ATCC) (Manassas, VA, USA) and the National Institute of General Medical Sciences (NIGMS) Human Genetic Cell Repository at the Coriell Cell Repositories (Camden, NJ, USA). Cells or cell lines derived from ovarian are particularly preferred because they may provide a more native post-translational processing. Particularly preferred are human ovarian cells.

Particular details of the transfection, expression and purification of recombinant proteins are well documented and are understood by those of skill in the art. Further details on the various technical aspects of each of the steps used in recombinant

production of foreign genes in bacterial cell expression systems can be found in a number of texts and laboratory manuals in the art. *See, e.g.*, Ausubel (1992), *supra*, Ausubel (1999), *supra*, Sambrook (1989), *supra*, and Sambrook (2001), *supra*.

Methods for introducing the vectors and nucleic acid molecules of the present invention into the host cells are well known in the art; the choice of technique will depend primarily upon the specific vector to be introduced and the host cell chosen.

Nucleic acid molecules and vectors may be introduced into prokaryotes, such as *E. coli,* in a number of ways. For instance, phage lambda vectors will typically be packaged using a packaging extract (*e.g.*, Gigapack® packaging extract, Stratagene, La Jolla, CA, USA), and the packaged virus used to infect *E. coli*.

Plasmid vectors will typically be introduced into chemically competent or electrocompetent bacterial cells. *E. coli* cells can be rendered chemically competent by treatment, *e.g.*, with $CaCl_2$, or a solution of Mg^{2+}, Mn^{2+}, Ca^{2+}, Rb^{+} or K^{+}, dimethyl sulfoxide, dithiothreitol, and hexamine cobalt (III), Hanahan, *J. Mol. Biol.* 166(4):557-80 (1983), and vectors introduced by heat shock. A wide variety of chemically competent strains are also available commercially (*e.g.*, Epicurian Coli® XL10-Gold® Ultracompetent Cells (Stratagene, La Jolla, CA, USA); DH5α competent cells (Clontech Laboratories, Palo Alto, CA, USA); and TOP10 Chemically Competent E. coli Kit (Invitrogen, Carlsbad, CA, USA)). Bacterial cells can be rendered electrocompetent to take up exogenous DNA by electroporation by various pre-pulse treatments; vectors are introduced by electroporation followed by subsequent outgrowth in selected media. An extensive series of protocols is provided by BioRad (Richmond, CA, USA).

Vectors can be introduced into yeast cells by spheroplasting, treatment with lithium salts, electroporation, or protoplast fusion. Spheroplasts are prepared by the action of hydrolytic enzymes such as a snail-gut extract, usually denoted Glusulase or Zymolyase, or an enzyme from *Arthrobacter luteus* to remove portions of the cell wall in the presence of osmotic stabilizers, typically 1 M sorbitol. DNA is added to the spheroplasts, and the mixture is co-precipitated with a solution of polyethylene glycol (PEG) and Ca^{2+}. Subsequently, the cells are resuspended in a solution of sorbitol, mixed with molten agar and then layered on the surface of a selective plate containing sorbitol.

For lithium-mediated transformation, yeast cells are treated with lithium acetate to permeabilize the cell wall, DNA is added and the cells are co-precipitated with PEG. The cells are exposed to a brief heat shock, washed free of PEG and lithium acetate, and

subsequently spread on plates containing ordinary selective medium. Increased frequencies of transformation are obtained by using specially-prepared single-stranded carrier DNA and certain organic solvents. Schiestl *et al.*, *Curr. Genet.* 16(5-6): 339-46 (1989).

For electroporation, freshly-grown yeast cultures are typically washed, suspended in an osmotic protectant, such as sorbitol, mixed with DNA, and the cell suspension pulsed in an electroporation device. Subsequently, the cells are spread on the surface of plates containing selective media. Becker *et al.*, *Methods Enzymol.* 194: 182-187 (1991). The efficiency of transformation by electroporation can be increased over 100-fold by using PEG, single-stranded carrier DNA and cells that are in late log-phase of growth. Larger constructs, such as YACs, can be introduced by protoplast fusion.

Mammalian and insect cells can be directly infected by packaged viral vectors, or transfected by chemical or electrical means. For chemical transfection, DNA can be coprecipitated with $CaPO_4$ or introduced using liposomal and nonliposomal lipid-based agents. Commercial kits are available for $CaPO_4$ transfection (CalPhos™ Mammalian Transfection Kit, Clontech Laboratories, Palo Alto, CA, USA), and lipid-mediated transfection can be practiced using commercial reagents, such as LIPOFECTAMINE™ 2000, LIPOFECTAMINE™ Reagent, CELLFECTIN® Reagent, and LIPOFECTIN® Reagent (Invitrogen, Carlsbad, CA, USA), DOTAP Liposomal Transfection Reagent, FuGENE 6, X-tremeGENE Q2, DOSPER, (Roche Molecular Biochemicals, Indianapolis, IN USA), Effectene™, PolyFect®, Superfect® (Qiagen, Inc., Valencia, CA, USA). Protocols for electroporating mammalian cells can be found in, for example, ; Norton *et al.* (eds.), Gene Transfer Methods: Introducing DNA into Living Cells and Organisms, BioTechniques Books, Eaton Publishing Co. (2000). Other transfection techniques include transfection by particle bombardment and microinjection. *See, e.g.*, Cheng *et al.*, *Proc. Natl. Acad. Sci. USA* 90(10): 4455-9 (1993); Yang *et al.*, *Proc. Natl. Acad. Sci. USA* 87(24): 9568-72 (1990).

Production of the recombinantly produced proteins of the present invention can optionally be followed by purification.

Purification of recombinantly expressed proteins is now well within the skill in the art and thus need not be detailed here. *See, e.g.*, Thorner *et al.* (eds.), Applications of Chimeric Genes and Hybrid Proteins, Part A: Gene Expression and Protein Purification (Methods in Enzymology, Vol. 326), Academic Press (2000); Harbin (ed.), Cloning, Gene

Expression and Protein Purification : Experimental Procedures and Process Rationale, Oxford Univ. Press (2001); Marshak *et al.*, Strategies for Protein Purification and Characterization: A Laboratory Course Manual, Cold Spring Harbor Laboratory Press (1996); and Roe (ed.), Protein Purification Applications, Oxford University Press (2001).

Briefly, however, if purification tags have been fused through use of an expression vector that appends such tags, purification can be effected, at least in part, by means appropriate to the tag, such as use of immobilized metal affinity chromatography for polyhistidine tags. Other techniques common in the art include ammonium sulfate fractionation, immunoprecipitation, fast protein liquid chromatography (FPLC), high performance liquid chromatography (HPLC), and preparative gel electrophoresis.

Polypeptides, including Fragments Muteins, Homologous Proteins, Allelic Variants, Analogs and Derivatives

Another aspect of the invention relates to polypeptides encoded by the nucleic acid molecules described herein. In a preferred embodiment, the polypeptide is an ovarian specific polypeptide (OSP). In an even more preferred embodiment, the polypeptide comprises an amino acid sequence of SEQ ID NO:129-295 or is derived from a polypeptide having the amino acid sequence of SEQ ID NO: 129-295. A polypeptide as defined herein may be produced recombinantly, as discussed *supra*, may be isolated from a cell that naturally expresses the protein, or may be chemically synthesized following the teachings of the specification and using methods well known to those having ordinary skill in the art.

Polypeptides of the present invention may also comprise a part or fragment of an OSP. In a preferred embodiment, the fragment is derived from a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO: 129-295. Polypeptides of the present invention comprising a part or fragment of an entire OSP may or may not be OSPs. For example, a full-length polypeptide may be ovarian-specific, while a fragment thereof may be found in other tissues as well as in ovarian. A polypeptide that is not an OSP, whether it is a fragment, analog, mutein, homologous protein or derivative, is nevertheless useful, especially for immunizing animals to prepare anti-OSP antibodies. In a preferred embodiment, the part or fragment is an OSP. Methods of determining whether a polypeptide of the present invention is an OSP are described *infra*.

Polypeptides of the present invention comprising fragments of at least 6 contiguous amino acids are also useful in mapping B cell and T cell epitopes of the reference protein. *See, e.g.*, Geysen *et al.*, *Proc. Natl. Acad. Sci. USA* 81: 3998-4002 (1984) and U.S. Patent Nos. 4,708,871 and 5,595,915, the disclosures of which are incorporated herein by reference in their entireties. Because the fragment need not itself be immunogenic, part of an immunodominant epitope, nor even recognized by native antibody, to be useful in such epitope mapping, all fragments of at least 6 amino acids of a polypeptide of the present invention have utility in such a study.

Polypeptides of the present invention comprising fragments of at least 8 contiguous amino acids, often at least 15 contiguous amino acids, are useful as immunogens for raising antibodies that recognize polypeptides of the present invention. *See, e.g.*, Lerner, Nature 299: 592-596 (1982); Shinnick *et al.*, *Annu. Rev. Microbiol.* 37: 425-46 (1983); Sutcliffe *et al.*, *Science* 219: 660-6 (1983). As further described in the above-cited references, virtually all 8-mers, conjugated to a carrier, such as a protein, prove immunogenic and are capable of eliciting antibody for the conjugated peptide; accordingly, all fragments of at least 8 amino acids of the polypeptides of the present invention have utility as immunogens.

Polypeptides comprising fragments of at least 8, 9, 10 or 12 contiguous amino acids are also useful as competitive inhibitors of binding of the entire polypeptide, or a portion thereof, to antibodies (as in epitope mapping), and to natural binding partners, such as subunits in a multimeric complex or to receptors or ligands of the subject protein; this competitive inhibition permits identification and separation of molecules that bind specifically to the polypeptide of interest. See U.S. Patent Nos. 5,539,084 and 5,783,674, incorporated herein by reference in their entireties.

The polypeptide of the present invention thus preferably is at least 6 amino acids in length, typically at least 8, 9, 10 or 12 amino acids in length, and often at least 15 amino acids in length. Often, the polypeptide of the present invention is at least 20 amino acids in length, even 25 amino acids, 30 amino acids, 35 amino acids, or 50 amino acids or more in length. Of course, larger polypeptides having at least 75 amino acids, 100 amino acids, or even 150 amino acids are also useful, and at times preferred.

One having ordinary skill in the art can produce fragments by truncating the nucleic acid molecule, *e.g.*, an OSNA, encoding the polypeptide and then expressing it recombinantly. Alternatively, one can produce a fragment by chemically synthesizing a

portion of the full-length polypeptide. One may also produce a fragment by enzymatically cleaving either a recombinant polypeptide or an isolated naturally occurring polypeptide. Methods of producing polypeptide fragments are well known in the art. *See*, *e.g.*, Sambrook (1989), *supra;* Sambrook (2001), *supra*; Ausubel (1992), *supra*; and Ausubel (1999), *supra*. In one embodiment, a polypeptide comprising only a fragment, preferably a fragment of an OSP, may be produced by chemical or enzymatic cleavage of an OSP polypeptide. In a preferred embodiment, a polypeptide fragment is produced by expressing a nucleic acid molecule of the present invention encoding a fragment, preferably of an OSP, in a host cell.

Polypeptides of the present invention are also inclusive of mutants, fusion proteins, homologous proteins and allelic variants.

A mutant protein, or mutein, may have the same or different properties compared to a naturally occurring polypeptide and comprises at least one amino acid insertion, duplication, deletion, rearrangement or substitution compared to the amino acid sequence of a native polypeptide. Small deletions and insertions can often be found that do not alter the function of a protein. Muteins may or may not be ovarian-specific. Preferably, the mutein is ovarian-specific. More preferably the mutein is a polypeptide that comprises at least one amino acid insertion, duplication, deletion, rearrangement or substitution compared to the amino acid sequence of SEQ ID NO: 129-295. Accordingly, in a preferred embodiment, the mutein is one that exhibits at least 50% sequence identity, more preferably at least 60% sequence identity, even more preferably at least 70%, yet more preferably at least 80% sequence identity to an OSP comprising an amino acid sequence of SEQ ID NO: 129-295. In a yet more preferred embodiment, the mutein exhibits at least 85%, more preferably 90%, even more preferably 95% or 96%, and yet more preferably at least 97%, 98%, 99% or 99.5% sequence identity to an OSP comprising an amino acid sequence of SEQ ID NO: 129-295.

A mutein may be produced by isolation from a naturally occurring mutant cell, tissue or organism. A mutein may be produced by isolation from a cell, tissue or organism that has been experimentally mutagenized. Alternatively, a mutein may be produced by chemical manipulation of a polypeptide, such as by altering the amino acid residue to another amino acid residue using synthetic or semi-synthetic chemical techniques. In a preferred embodiment, a mutein is produced from a host cell comprising a mutated nucleic acid molecule compared to the naturally occurring nucleic acid molecule. For instance,

one may produce a mutein of a polypeptide by introducing one or more mutations into a nucleic acid molecule of the invention and then expressing it recombinantly. These mutations may be targeted, in which particular encoded amino acids are altered, or may be untargeted, in which random encoded amino acids within the polypeptide are altered. Muteins with random amino acid alterations can be screened for a particular biological activity or property, particularly whether the polypeptide is ovarian-specific, as described below. Multiple random mutations can be introduced into the gene by methods well known to the art, *e.g.*, by error-prone PCR, shuffling, oligonucleotide-directed mutagenesis, assembly PCR, sexual PCR mutagenesis, *in vivo* mutagenesis, cassette mutagenesis, recursive ensemble mutagenesis, exponential ensemble mutagenesis and site-specific mutagenesis. Methods of producing muteins with targeted or random amino acid alterations are well known in the art. *See, e.g.*, Sambrook (1989), *supra;* Sambrook (2001), *supra*; Ausubel (1992), *supra*; and Ausubel (1999), as well as U.S. Patent No. 5,223,408, which is herein incorporated by reference in its entirety.

The invention also contemplates polypeptides that are homologous to a polypeptide of the invention. In a preferred embodiment, the polypeptide is homologous to an OSP. In an even more preferred embodiment, the polypeptide is homologous to an OSP selected from the group having an amino acid sequence of SEQ ID NO: 129-295. By homologous polypeptide it is meant one that exhibits significant sequence identity to an OSP, preferably an OSP having an amino acid sequence of SEQ ID NO: 129-295. By significant sequence identity it is meant that the homologous polypeptide exhibits at least 50% sequence identity, more preferably at least 60% sequence identity, even more preferably at least 70%, yet more preferably at least 80% sequence identity to an OSP comprising an amino acid sequence of SEQ ID NO: 129-295. More preferred are homologous polypeptides exhibiting at least 85%, more preferably 90%, even more preferably 95% or 96%, and yet more preferably at least 97% or 98% sequence identity to an OSP comprising an amino acid sequence of SEQ ID NO: 129-295. Most preferably, the homologous polypeptide exhibits at least 99%, more preferably 99.5%, even more preferably 99.6%, 99.7%, 99.8% or 99.9% sequence identity to an OSP comprising an amino acid sequence of SEQ ID NO: 129-295. In a preferred embodiment, the amino acid substitutions of the homologous polypeptide are conservative amino acid substitutions as discussed supra.

Homologous polypeptides of the present invention also comprise polypeptide encoded by a nucleic acid molecule that selectively hybridizes to an OSNA or an antisense sequence thereof. In this embodiment, it is preferred that the homologous polypeptide be encoded by a nucleic acid molecule that hybridizes to an OSNA under low stringency, moderate stringency or high stringency conditions, as defined herein. More preferred is a homologous polypeptide encoded by a nucleic acid sequence which hybridizes to a OSNA selected from the group consisting of SEQ ID NO: 1-128 or a homologous polypeptide encoded by a nucleic acid molecule that hybridizes to a nucleic acid molecule that encodes an OSP, preferably an OSP of SEQ ID NO:129-295 under low stringency, moderate stringency or high stringency conditions, as defined herein.

Homologous polypeptides of the present invention may be naturally occurring and derived from another species, especially one derived from another primate, such as chimpanzee, gorilla, rhesus macaque, or baboon, wherein the homologous polypeptide comprises an amino acid sequence that exhibits significant sequence identity to that of SEQ ID NO: 129-295. The homologous polypeptide may also be a naturally occurring polypeptide from a human, when the OSP is a member of a family of polypeptides. The homologous polypeptide may also be a naturally occurring polypeptide derived from a non-primate, mammalian species, including without limitation, domesticated species, *e.g.*, dog, cat, mouse, rat, rabbit, guinea pig, hamster, cow, horse, goat or pig. The homologous polypeptide may also be a naturally occurring polypeptide derived from a non-mammalian species, such as birds or reptiles. The naturally occurring homologous protein may be isolated directly from humans or other species. Alternatively, the nucleic acid molecule encoding the naturally occurring homologous polypeptide may be isolated and used to express the homologous polypeptide recombinantly. The homologous polypeptide may also be one that is experimentally produced by random mutation of a nucleic acid molecule and subsequent expression of the nucleic acid molecule. Alternatively, the homologous polypeptide may be one that is experimentally produced by directed mutation of one or more codons to alter the encoded amino acid of an OSP. In a preferred embodiment, the homologous polypeptide encodes a polypeptide that is an OSP.

Relatedness of proteins can also be characterized using a second functional test, such as the ability of a first protein competitively to inhibit the binding of a second protein to an antibody. It is, therefore, another aspect of the present invention to provide isolated polypeptides not only identical in sequence to those described with particularity herein,

but also to provide isolated polypeptides ("cross-reactive proteins") that competitively inhibit the binding of antibodies to all or to a portion of the isolated polypeptides of the present invention. Such competitive inhibition can readily be determined using immunoassays well known in the art.

As discussed above, single nucleotide polymorphisms (SNPs) occur frequently in eukaryotic genomes, and the sequence determined from one individual of a species may differ from other allelic forms present within the population. Thus, polypeptides of the present invention are also inclusive of those encoded by an allelic variant of a nucleic acid molecule encoding an OSP. In this embodiment, it is preferred that the polypeptide be encoded by an allelic variant of a gene that encodes a polypeptide having the amino acid sequence selected from the group consisting of SEQ ID NO: 129-295. More preferred is that the polypeptide be encoded by an allelic variant of a gene that has the nucleic acid sequence selected from the group consisting of SEQ ID NO: 1-128.

Polypeptides of the present invention are also inclusive of derivative polypeptides encoded by a nucleic acid molecule according to the instant invention. In this embodiment, it is preferred that the polypeptide be an OSP. Also preferred are derivative polypeptides having an amino acid sequence selected from the group consisting of SEQ ID NO: 129-295 and which has been acetylated, carboxylated, phosphorylated, glycosylated, ubiquitinated or post-translationally modified in another manner. In another preferred embodiment, the derivative has been labeled with, *e.g.*, radioactive isotopes such as ^{125}I, ^{32}P, ^{35}S, and ^{3}H. In another preferred embodiment, the derivative has been labeled with fluorophores, chemiluminescent agents, enzymes, and antiligands that can serve as specific binding pair members for a labeled ligand.

Polypeptide modifications are well known to those of skill and have been described in great detail in the scientific literature. Several particularly common modifications, glycosylation, lipid attachment, sulfation, gamma-carboxylation of glutamic acid residues, hydroxylation and ADP-ribosylation, for instance, are described in most basic texts, such as, for instance Creighton, Protein Structure and Molecular Properties, 2nd ed., W. H. Freeman and Company (1993). Many detailed reviews are available on this subject, such as, for example, those provided by Wold, in Johnson (ed.), Posttranslational Covalent Modification of Proteins, pgs. 1-12, Academic Press (1983); Seifter *et al.*, *Meth. Enzymol.* 182: 626-646 (1990) and Rattan *et al.*, *Ann. N.Y. Acad. Sci.* 663: 48-62 (1992).

One may determine whether a polypeptide of the invention is likely to be post-translationally modified by analyzing the sequence of the polypeptide to determine if there are peptide motifs indicative of sites for post-translational modification. There are a number of computer programs that permit prediction of post-translational modifications. See, e.g., expasy.org (accessed November 11, 2002) of the world wide web, which includes PSORT, for prediction of protein sorting signals and localization sites, SignalP, for prediction of signal peptide cleavage sites, MITOPROT and Predotar, for prediction of mitochondrial targeting sequences, NetOGlyc, for prediction of type O-glycosylation sites in mammalian proteins, big-PI Predictor and DGPI, for prediction of prenylation-anchor and cleavage sites, and NetPhos, for prediction of Ser, Thr and Tyr phosphorylation sites in eukaryotic proteins. Other computer programs, such as those included in GCG, also may be used to determine post-translational modification peptide motifs.

General examples of types of post-translational modifications include, but are not limited to: (Z)-dehydrobutyrine; 1-chondroitin sulfate-L-aspartic acid ester; 1'-glycosyl-L-tryptophan; 1'-phospho-L-histidine; 1-thioglycine; 2'-(S-L-cysteinyl)-L-histidine; 2'-[3-carboxamido (trimethylammonio)propyl]-L-histidine; 2'-alpha-mannosyl-L-tryptophan; 2-methyl-L-glutamine; 2-oxobutanoic acid; 2-pyrrolidone carboxylic acid; 3'-(1'-L-histidyl)-L-tyrosine; 3'-(8alpha-FAD)-L-histidine; 3'-(S-L-cysteinyl)-L-tyrosine; 3', 3",5'-triiodo-L-thyronine; 3'-4'-phospho-L-tyrosine; 3-hydroxy-L-proline; 3'-methyl-L-histidine; 3-methyl-L-lanthionine; 3'-phospho-L-histidine; 4'-(L-tryptophan)-L-tryptophyl quinone; 42 N-cysteinyl-glycosylphosphatidylinositolethanolamine; 43 -(T-L-histidyl)-L-tyrosine; 4-hydroxy-L-arginine; 4-hydroxy-L-lysine; 4-hydroxy-L-proline; 5'-(N6-L-lysine)-L-topaquinone; 5-hydroxy-L-lysine; 5-methyl-L-arginine; alpha-l-microglobulin-Ig alpha complex chromophore; bis-L-cysteinyl bis-L-histidino diiron disulfide; bis-L--cysteinyl-L-N3'-histidino-L-serinyl tetrairon' tetrasulfide; chondroitin sulfate D-glucuronyl-D-galactosyl-D-galactosyl-D-xylosyl-L-serine; D-alanine; D-allo-isoleucine; D-asparagine; dehydroalanine; dehydrotyrosine; dermatan 4-sulfate D-glucuronyl-D-galactosyl-D-galactosyl-D-xylosyl-L-serine; D-glucuronyl-N-glycine; dipyrrolylmethanemethyl-L-cysteine; D-leucine; D-methionine; D-phenylalanine; D-serine; D-tryptophan; glycine amide; glycine oxazolecarboxylic acid; glycine thiazolecarboxylic acid; heme P450-bis-L-cysteine-L-tyrosine; heme-bis-L-cysteine; hemediol-L-aspartyl ester-L-glutamyl ester; hemediol-L-aspartyl ester-L-glutamyl ester-L-methionine sulfonium; heme-L-cysteine; heme-L-histidine; heparan sulfate D-glucuronyl-D-galactosyl-D-galactosyl-D-xylosyl-L-

serine; heme P450-bis-L-cysteine-L-lysine; hexakis-L-cysteinyl hexairon hexasulfide; keratan sulfate D-glucuronyl-D-galactosyl-D-galactosyl-D-xylosyl-L-threonine; L oxoalanine- lactic acid; L phenyllactic acid; l'-(8alpha-FAD)-L-histidine; L-2'.4',5'-topaquinone; L-3',4'-dihydroxyphenylalanine; L-3'.4'.5'-trihydroxyphenylalanine; L-4'-bromophenylalanine; L-6'-bromotryptophan; L-alanine amide; L-alanyl imidazolinone glycine; L-allysine; L-arginine amide; L-asparagine amide; L-aspartic 4-phosphoric anhydride; L-aspartic acid 1-amide; L-beta-methylthioaspartic acid; L-bromohistidine; L-citrulline; L-cysteine amide; L-cysteine glutathione disulfide; L-cysteine methyl disulfide; L-cysteine methyl ester; L-cysteine oxazolecarboxylic acid; L-cysteine oxazolinecarboxylic acid; L-cysteine persulfide; L-cysteine sulfenic acid; L-cysteine sulfinic acid; L-cysteine thiazolecarboxylic acid; L-cysteinyl homocitryl molybdenum-heptairon-nonasulfide; L-cysteinyl imidazolinone glycine; L-cysteinyl molybdopterin; L-cysteinyl molybdopterin guanine dinucleotide; L-cystine; L-erythro-beta-hydroxyasparagine; L-erythro-beta-hydroxyaspartic acid; L-gamma-carboxyglutamic acid; L-glutamic acid 1-amide; L-glutamic acid 5-methyl ester; L-glutamine amide; L-glutamyl 5-glycerylphosphorylethanolarnine; L-histidine amide; L-isoglutamyl-polyglutamic acid; L-isoglutamyl-polyglycine; L-isoleucine amide; L-lanthionine; L-leucine amide; L-lysine amide; L-lysine thiazolecarboxylic acid; L-lysinoalanine; L-methionine amide; L-methionine sulfone; L-phenyalanine thiazolecarboxylic acid; L-phenylalanine amide; L-proline amide; L-selenocysteine; L-selenocysteinyl molybdopterin guanine dinucleotide; L-serine amide; L-serine thiazolecarboxylic acid; L-seryl imidazolinone glycine; L-T-bromophenylalanine; L-T-bromophenylalanine; L-threonine amide; L-thyroxine; L-tryptophan amide; L-tryptophyl quinone; L-tyrosine amide; L-valine amide; meso-lanthionine; N-(L-glutamyl)-L-tyrosine; N-(L-isoaspartyl)-glycine; N-(L-isoaspartyl)-L-cysteine; N,N,N-trimethyl-L-alanine; N,N-dimethyl-L-proline; N2-acetyl-L-lysine; N2-succinyl-L-tryptophan; N4-(ADP-ribosyl)-L-asparagine; N4-glycosyl-L-asparagine; N4-hydroxymethyl-L-asparagine; N4-methyl-L-asparagine; N5-methyl-L-glutamine; N6- 1 -carboxyethyl-L-lysine; N6-(4-amino hydroxybutyl)-L-lysine; N6-(L-isoglutamyl)-L-lysine; N6-(phospho-5'-adenosine)-L-lysine; N6-(phospho-5'-guanosine)-L-tysine; N6,N6,N6-trimethyl-L-lysine; N6,N6-dimethyl-L-lysine; N6-acetyl-L-lysine; N6-biotinyl-L-lysine; N6-carboxy-L-lysine; N6-formyl-L-lysine; N6-glycyl-L-lysine; N6-lipoyl-L-lysine; N6-methyl-L-lysine; N6-methyl-N6-poly(N-methyl-propylamine)-L-lysine; N6-mureinyl-L-lysine; N6-myristoyl-L-lysine; N6-palmitoyl-L-lysine; N6-pyridoxal

phosphate-L-lysine; N6-pyruvic acid 2-iminyl-L-lysine; N6-retinal-L-lysine; N-acetylglycine; N-acetyl-L-glutamine; N-acetyl-L-alanine; N-acetyl-L-aspartic acid; N-acetyl-L-cysteine; N-acetyl-L-glutamic acid; N-acetyl-L-isoleucine; N-acetyl-L-methionine; N-acetyl-L-proline; N-acetyl-L-serine; N-acetyl-L-threonine; N-acetyl-L-tyrosine; N-acetyl-L-valine; N-alanyl-glycosylphosphatidylinositolethanolamine; N-asparaginyl-glycosylphosphatidylinositolethanolarnine; N-aspartyl-glycosylphosphatidylinositolethanolamine; N-formylglycine; N-formyl-L-methionine; N-glycyl-glycosylphosphatidylinositolethanolamine; N-L-glutamyl-poly-L-glutamic acid; N-methylglycine; N-methyl-L-alanine; N-methyl-L-methionine; N-methyl-L-phenylalanine; N-myristoyl-glycine; N-palmitoyl-L-cysteine; N-pyruvic acid 2-iminyl-L-cysteine; N-pyruvic acid 2-iminyl-L-valine; N-seryl-glycosylphosphatidylinositolethanolamine; N-seryl-glycosyOSPhingolipidinositolethanolamine; O-(ADP-ribosyl)-L-serine; O-(phospho-5'-adenosine)-L-threonine; O-(phospho-5'-DNA)-L-serine; O-(phospho-5'-DNA)-L-threonine; O-(phospho-5'rRNA)-L-serine; O-(phosphoribosyl dephospho-coenzyme A)-L-serine; O-(sn-l-glycerophosphoryl)-L-serine; O4'-(8alpha-FAD)-L-tyrosine; O4'-(phospho-5'-adenosine)-L-tyrosine; O4'-(phospho-5'-DNA)-L-tyrosine; O4'-(phospho-5'-RNA)-L-tyrosine; O4'-(phospho-5'-uridine)-L-tyrosine; O4-glycosyl-L-hydroxyproline; O4'-glycosyl-L-tyrosine; O4'-sulfo-L-tyrosine; O5-glycosyl-L-hydroxylysine; O-glycosyl-L-serine; O-glycosyl-L-threonine; omega-N-(ADP-ribosyl)-L-arginine; omega-N-omega-N'-dimethyl-L-arginine; omega-N-methyl-L-arginine; omega-N-omega-N-dimethyl-L-arginine; omega-N-phospho-L-arginine; O'octanoyl-L-serine; O-palmitoyl-L-serine; O-palmitoyl-L-threonine; O-phospho-L-serine; O-phospho-L-threonine; O-phosphopantetheine-L-serine; phycoerythrobilin-bis-L-cysteine; phycourobilin-bis-L-cysteine; pyrroloquinoline quinone; pyruvic acid; S hydroxycinnamyl-L-cysteine; S-(2-aminovinyl) methyl-D-eysteine; S-(2-aminovinyl)-D-cysteine; S-(6-FW-L-cysteine; S-(8alpha-FAD)-L-cysteine; S-(ADP-ribosyl)-L-cysteine; S-(L-isoglutamyl)-L-cysteine; S-12-hydroxyfarnesyl-L-cysteine; S-acetyl-L-cysteine; S-diacylglycerol-L-cysteine; S-diphytanylglycerot diether-L-cysteine; S-farnesyl-L-cysteine; S-geranylgeranyl-L-cysteine; S-glycosyl-L-cysteine; S-glycyl-L-cysteine; S-methyl-L-cysteine; S-nitrosyl-L-cysteine; S-palmitoyl-L-cysteine; S-phospho-L-cysteine; S-phycobiliviolin-L-cysteine; S-phycocyanobilin-L-cysteine; S-phycoerythrobilin-L-cysteine; S-phytochromobilin-L-cysteine; S-selenyl-L-cysteine; S-sulfo-L-cysteine; tetrakis-L-cysteinyl diiron disulfide; tetrakis-L-cysteinyl iron; tetrakis-L-cysteinyl tetrairon tetrasulfide; trans-2,3-cis 4-

dihydroxy-L-proline; tris-L-cysteinyl triiron tetrasulfide; tris-L-cysteinyl triiron trisulfide; tris-L-cysteinyl-L-aspartato tetrairon tetrasulfide; tris-L-cysteinyl-L-cysteine persulfido-bis-L-glutamato-L-histidino tetrairon disulfide trioxide; tris-L-cysteinyl-L-N3'-histidino tetrairon tetrasulfide; tris-L-cysteinyl-L-Nl'-histidino tetrairon tetrasulfide; and tris-L-cysteinyl-L-serinyl tetrairon tetrasulfide.

Additional examples of PTMs may be found in web sites such as the Delta Mass database based on Krishna, R. G. and F. Wold (1998). Posttranslational Modifications. Proteins - Analysis and Design. R. H. Angeletti. San Diego, Academic Press. 1: 121-206; Methods in Enzymology, 193, J.A. McClosky (ed) (1990), pages 647-660; Methods in Protein Sequence Analysis edited by Kazutomo Imahori and Fumio Sakiyama, Plenum Press, (1993) "Post-translational modifications of proteins" R.G. Krishna and F. Wold pages 167-172; "GlycoSuiteDB: a new curated relational database of glycoprotein glycan structures and their biological sources" Cooper et al. Nucleic Acids Res. 29; 332-335 (2001) “O-GLYCBASE version 4.0: a revised database of O-glycosylated proteins” Gupta et al. Nucleic Acids Research, 27: 370-372 (1999); and "PhosphoBase, a database of phosphorylation sites: release 2.0.", Kreegipuu et al.Nucleic Acids Res 27(1):237-239 (1999) see also,WO 02/21139A2, the disclosure of which is incorporated herein by reference in its entirety.

Tumorigenesis is often accompanied by alterations in the post-translational modifications of proteins. Thus, in another embodiment, the invention provides polypeptides from cancerous cells or tissues that have altered post-translational modifications compared to the post-translational modifications of polypeptides from normal cells or tissues. A number of altered post-translational modifications are known. One common alteration is a change in phosphorylation state, wherein the polypeptide from the cancerous cell or tissue is hyperphosphorylated or hypophosphorylated compared to the polypeptide from a normal tissue, or wherein the polypeptide is phosphorylated on different residues than the polypeptide from a normal cell. Another common alteration is a change in glycosylation state, wherein the polypeptide from the cancerous cell or tissue has more or less glycosylation than the polypeptide from a normal tissue, and/or wherein the polypeptide from the cancerous cell or tissue has a different type of glycosylation than the polypeptide from a noncancerous cell or tissue. Changes in glycosylation may be critical because carbohydrate-protein and carbohydrate-carbohydrate interactions are important in cancer cell progression, dissemination and invasion. See, e.g., Barchi, *Curr.*

Pharm. Des. 6: 485-501 (2000), Verma, *Cancer Biochem. Biophys.* 14: 151-162 (1994) and Dennis et al., *Bioessays* 5: 412-421 (1999).

Another post-translational modification that may be altered in cancer cells is prenylation. Prenylation is the covalent attachment of a hydrophobic prenyl group (either farnesyl or geranylgeranyl) to a polypeptide. Prenylation is required for localizing a protein to a cell membrane and is often required for polypeptide function. For instance, the Ras superfamily of GTPase signalling proteins must be prenylated for function in a cell. See, e.g., Prendergast et al., *Semin. Cancer Biol.* 10: 443-452 (2000) and Khwaja et al., *Lancet* 355: 741-744 (2000).

Other post-translation modifications that may be altered in cancer cells include, without limitation, polypeptide methylation, acetylation, arginylation or racemization of amino acid residues. In these cases, the polypeptide from the cancerous cell may exhibit either increased or decreased amounts of the post-translational modification compared to the corresponding polypeptides from noncancerous cells.

Other polypeptide alterations in cancer cells include abnormal polypeptide cleavage of proteins and aberrant protein-protein interactions. Abnormal polypeptide cleavage may be cleavage of a polypeptide in a cancerous cell that does not usually occur in a normal cell, or a lack of cleavage in a cancerous cell, wherein the polypeptide is cleaved in a normal cell. Aberrant protein-protein interactions may be either covalent cross-linking or non-covalent binding between proteins that do not normally bind to each other. Alternatively, in a cancerous cell, a protein may fail to bind to another protein to which it is bound in a noncancerous cell. Alterations in cleavage or in protein-protein interactions may be due to over- or underproduction of a polypeptide in a cancerous cell compared to that in a normal cell, or may be due to alterations in post-translational modifications (see above) of one or more proteins in the cancerous cell. See, e.g., Henschen-Edman, *Ann. N.Y. Acad. Sci.* 936: 580-593 (2001).

Alterations in polypeptide post-translational modifications, as well as changes in polypeptide cleavage and protein-protein interactions, may be determined by any method known in the art. For instance, alterations in phosphorylation may be determined by using anti-phosphoserine, anti-phosphothreonine or anti-phosphotyrosine antibodies or by amino acid analysis. Glycosylation alterations may be determined using antibodies specific for different sugar residues, by carbohydrate sequencing, or by alterations in the size of the glycoprotein, which can be determined by, e.g., SDS polyacrylamide gel electrophoresis

(PAGE). Other alterations of post-translational modifications, such as prenylation, racemization, methylation, acetylation and arginylation, may be determined by chemical analysis, protein sequencing, amino acid analysis, or by using antibodies specific for the particular post-translational modifications. Changes in protein-protein interactions and in polypeptide cleavage may be analyzed by any method known in the art including, without limitation, non-denaturing PAGE (for non-covalent protein-protein interactions), SDS PAGE (for covalent protein-protein interactions and protein cleavage), chemical cleavage, protein sequencing or immunoassays.

In another embodiment, the invention provides polypeptides that have been post-translationally modified. In one embodiment, polypeptides may be modified enzymatically or chemically, by addition or removal of a post-translational modification. For example, a polypeptide may be glycosylated or deglycosylated enzymatically. Similarly, polypeptides may be phosphorylated using a purified kinase, such as a MAP kinase (e.g, p38, ERK, or JNK) or a tyrosine kinase (e.g., Src or erbB2). A polypeptide may also be modified through synthetic chemistry. Alternatively, one may isolate the polypeptide of interest from a cell or tissue that expresses the polypeptide with the desired post-translational modification. In another embodiment, a nucleic acid molecule encoding the polypeptide of interest is introduced into a host cell that is capable of post-translationally modifying the encoded polypeptide in the desired fashion. If the polypeptide does not contain a motif for a desired post-translational modification, one may alter the post-translational modification by mutating the nucleic acid sequence of a nucleic acid molecule encoding the polypeptide so that it contains a site for the desired post-translational modification. Amino acid sequences that may be post-translationally modified are known in the art. See, e.g., the programs described above on the website expasy.org of the world wide web. The nucleic acid molecule may also be introduced into a host cell that is capable of post-translationally modifying the encoded polypeptide. Similarly, one may delete sites that are post-translationally modified by either mutating the nucleic acid sequence so that the encoded polypeptide does not contain the post-translational modification motif, or by introducing the native nucleic acid molecule into a host cell that is not capable of post-translationally modifying the encoded polypeptide.

It will be appreciated, as is well known and as noted above, that polypeptides are not always entirely linear. For instance, polypeptides may be branched as a result of ubiquitination, and they may be circular, with or without branching, generally as a result

of posttranslation events, including natural processing events and events brought about by human manipulation which do not occur naturally. Circular, branched and branched circular polypeptides may be synthesized by non-translation natural processes and by entirely synthetic methods, as well. Modifications can occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. In fact, blockage of the amino or carboxyl group in a polypeptide, or both, by a covalent modification, is common in naturally occurring and synthetic polypeptides and such modifications may be present in polypeptides of the present invention, as well. For instance, the amino terminal residue of polypeptides made in *E. coli*, prior to proteolytic processing, almost invariably will be N-formylmethionine.

Useful post-synthetic (and post-translational) modifications include conjugation to detectable labels, such as fluorophores. A wide variety of amine-reactive and thiol-reactive fluorophore derivatives have been synthesized that react under nondenaturing conditions with N-terminal amino groups and epsilon amino groups of lysine residues, on the one hand, and with free thiol groups of cysteine residues, on the other.

Kits are available commercially that permit conjugation of proteins to a variety of amine-reactive or thiol-reactive fluorophores: Molecular Probes, Inc. (Eugene, OR, USA), *e.g.*, offers kits for conjugating proteins to Alexa Fluor 350, Alexa Fluor 430, Fluorescein-EX, Alexa Fluor 488, Oregon Green 488, Alexa Fluor 532, Alexa Fluor 546, Alexa Fluor 546, Alexa Fluor 568, Alexa Fluor 594, and Texas Red-X.

A wide variety of other amine-reactive and thiol-reactive fluorophores are available commercially (Molecular Probes, Inc., Eugene, OR, USA), including Alexa Fluor® 350, Alexa Fluor® 488, Alexa Fluor® 532, Alexa Fluor® 546, Alexa Fluor® 568, Alexa Fluor® 594, Alexa Fluor® 647 (monoclonal antibody labeling kits available from Molecular Probes, Inc., Eugene, OR, USA), BODIPY dyes, such as BODIPY 493/503, BODIPY FL, BODIPY R6G, BODIPY 530/550, BODIPY TMR, BODIPY 558/568, BODIPY 558/568, BODIPY 564/570, BODIPY 576/589, BODIPY 581/591, BODIPY TR, BODIPY 630/650, BODIPY 650/665, Cascade Blue, Cascade Yellow, Dansyl, lissamine rhodamine B, Marina Blue, Oregon Green 488, Oregon Green 514, Pacific Blue, rhodamine 6G, rhodamine green, rhodamine red, tetramethylrhodamine, Texas Red (available from Molecular Probes, Inc., Eugene, OR, USA).

The polypeptides of the present invention can also be conjugated to fluorophores, other proteins, and other macromolecules, using bifunctional linking reagents. Common

homobifunctional reagents include, *e.g.*, APG, AEDP, BASED, BMB, BMDB, BMH, BMOE, BM[PEO]3, BM[PEO]4, BS3, BSOCOES, DFDNB, DMA, DMP, DMS, DPDPB, DSG, DSP (Lomant's Reagent), DSS, DST, DTBP, DTME, DTSSP, EGS, HBVS, Sulfo-BSOCOES, Sulfo-DST, Sulfo-EGS (all available from Pierce, Rockford, IL, USA); common heterobifunctional cross-linkers include ABH, AMAS, ANB-NOS, APDP, ASBA, BMPA, BMPH, BMPS, EDC, EMCA, EMCH, EMCS, KMUA, KMUH, GMBS, LC-SMCC, LC-SPDP, MBS, M2C2H, MPBH, MSA, NHS-ASA, PDPH, PMPI, SADP, SAED, SAND, SANPAH, SASD, SATP, SBAP, SFAD, SIA, SIAB, SMCC, SMPB, SMPH, SMPT, SPDP, Sulfo-EMCS, Sulfo-GMBS, Sulfo-HSAB, Sulfo-KMUS, Sulfo-LC-SPDP, Sulfo-MBS, Sulfo-NHS-LC-ASA, Sulfo-SADP, Sulfo-SANPAH, Sulfo-SIAB, Sulfo-SMCC, Sulfo-SMPB, Sulfo-LC-SMPT, SVSB, TFCS (all available Pierce, Rockford, IL, USA).

Polypeptides of the present invention, including full length polypeptides, fragments and fusion proteins, can be conjugated, using such cross-linking reagents, to fluorophores that are not amine- or thiol-reactive. Other labels that usefully can be conjugated to polypeptides of the present invention include radioactive labels, echosonographic contrast reagents, and MRI contrast agents.

Polypeptides of the present invention, including full length polypeptides, fragments and fusion proteins, can also usefully be conjugated using cross-linking agents to carrier proteins, such as KLH, bovine thyroglobulin, and even bovine serum albumin (BSA), to increase immunogenicity for raising anti-OSP antibodies.

Polypeptides of the present invention, including full length polypeptides, fragments and fusion proteins, can also usefully be conjugated to polyethylene glycol (PEG); PEGylation increases the serum half life of proteins administered intravenously for replacement therapy. Delgado *et al.*, *Crit. Rev. Ther. Drug Carrier Syst.* 9(3-4): 249-304 (1992); Scott *et al.*, *Curr. Pharm. Des.* 4(6): 423-38 (1998); DeSantis *et al.*, *Curr. Opin. Biotechnol.* 10(4): 324-30 (1999). PEG monomers can be attached to the protein directly or through a linker, with PEGylation using PEG monomers activated with tresyl chloride (2,2,2-trifluoroethanesulphonyl chloride) permitting direct attachment under mild conditions.

Polypeptides of the present invention are also inclusive of analogs of a polypeptide encoded by a nucleic acid molecule according to the instant invention. In a preferred embodiment, this polypeptide is an OSP. In a more preferred embodiment, this

polypeptide is derived from a polypeptide having part or all of the amino acid sequence of SEQ ID NO: 129-295. Also preferred is an analog polypeptide comprising one or more substitutions of non-natural amino acids or non-native inter-residue bonds compared to the naturally occurring polypeptide. In one embodiment, the analog is structurally similar to an OSP, but one or more peptide linkages is replaced by a linkage selected from the group consisting of --CH_2NH--, --CH_2S--, --CH_2-CH_2--, --CH=CH--(cis and trans), --$COCH_2$--, --$CH(OH)CH_2$-- and –CH_2SO--. In another embodiment, the analog comprises substitution of one or more amino acids of an OSP with a D-amino acid of the same type or other non-natural amino acid in order to generate more stable peptides. D-amino acids can readily be incorporated during chemical peptide synthesis: peptides assembled from D-amino acids are more resistant to proteolytic attack; incorporation of D-amino acids can also be used to confer specific three-dimensional conformations on the peptide. Other amino acid analogues commonly added during chemical synthesis include ornithine, norleucine, phosphorylated amino acids (typically phosphoserine, phosphothreonine, phosphotyrosine), L-malonyltyrosine, a non-hydrolyzable analog of phosphotyrosine (*see, e.g.,* Kole *et al.*, *Biochem. Biophys. Res. Com.* 209: 817-821 (1995)), and various halogenated phenylalanine derivatives.

Non-natural amino acids can be incorporated during solid phase chemical synthesis or by recombinant techniques, although the former is typically more common. Solid phase chemical synthesis of peptides is well established in the art. Procedures are described, *inter alia*, in Chan *et al.* (eds.), Fmoc Solid Phase Peptide Synthesis: A Practical Approach (Practical Approach Series), Oxford Univ. Press (March 2000); Jones, Amino Acid and Peptide Synthesis (Oxford Chemistry Primers, No 7), Oxford Univ. Press (1992); and Bodanszky, Principles of Peptide Synthesis (Springer Laboratory), Springer Verlag (1993).

Amino acid analogues having detectable labels are also usefully incorporated during synthesis to provide derivatives and analogs. Biotin, for example can be added using biotinoyl-(9-fluorenylmethoxycarbonyl)-L-lysine (FMOC biocytin) (Molecular Probes, Eugene, OR, USA). Biotin can also be added enzymatically by incorporation into a fusion protein of an *E. coli* BirA substrate peptide. The FMOC and *t*BOC derivatives of dabcyl-L-lysine (Molecular Probes, Inc., Eugene, OR, USA) can be used to incorporate the dabcyl chromophore at selected sites in the peptide sequence during synthesis. The

aminonaphthalene derivative EDANS, the most common fluorophore for pairing with the dabcyl quencher in fluorescence resonance energy transfer (FRET) systems, can be introduced during automated synthesis of peptides by using EDANS-FMOC-L-glutamic acid or the corresponding *t*BOC derivative (both from Molecular Probes, Inc., Eugene, OR, USA). Tetramethylrhodamine fluorophores can be incorporated during automated FMOC synthesis of peptides using (FMOC)-TMR-L-lysine (Molecular Probes, Inc. Eugene, OR, USA).

Other useful amino acid analogues that can be incorporated during chemical synthesis include aspartic acid, glutamic acid, lysine, and tyrosine analogues having allyl side-chain protection (Applied Biosystems, Inc., Foster City, CA, USA); the allyl side chain permits synthesis of cyclic, branched-chain, sulfonated, glycosylated, and phosphorylated peptides.

A large number of other FMOC-protected non-natural amino acid analogues capable of incorporation during chemical synthesis are available commercially, including, *e.g.*, Fmoc-2-aminobicyclo[2.2.1]heptane-2-carboxylic acid, Fmoc-3-endo-aminobicyclo[2.2.1]heptane-2-endo-carboxylic acid, Fmoc-3-exo-aminobicyclo[2.2.1]heptane-2-exo-carboxylic acid, Fmoc-3-endo-amino-bicyclo[2.2.1]hept-5-ene-2-endo-carboxylic acid, Fmoc-3-exo-amino-bicyclo[2.2.1]hept-5-ene-2-exo-carboxylic acid, Fmoc-cis-2-amino-1-cyclohexanecarboxylic acid, Fmoc-trans-2-amino-1-cyclohexanecarboxylic acid, Fmoc-1-amino-1-cyclopentanecarboxylic acid, Fmoc-cis-2-amino-1-cyclopentanecarboxylic acid, Fmoc-1-amino-1-cyclopropanecarboxylic acid, Fmoc-D-2-amino-4-(ethylthio)butyric acid, Fmoc-L-2-amino-4-(ethylthio)butyric acid, Fmoc-L-buthionine, Fmoc-S-methyl-L-Cysteine, Fmoc-2-aminobenzoic acid (anthranillic acid), Fmoc-3-aminobenzoic acid, Fmoc-4-aminobenzoic acid, Fmoc-2-aminobenzophenone-2'-carboxylic acid, Fmoc-N-(4-aminobenzoyl)-β-alanine, Fmoc-2-amino-4,5-dimethoxybenzoic acid, Fmoc-4-aminohippuric acid, Fmoc-2-amino-3-hydroxybenzoic acid, Fmoc-2-amino-5-hydroxybenzoic acid, Fmoc-3-amino-4-hydroxybenzoic acid, Fmoc-4-amino-3-hydroxybenzoic acid, Fmoc-4-amino-2-hydroxybenzoic acid, Fmoc-5-amino-2-hydroxybenzoic acid, Fmoc-2-amino-3-methoxybenzoic acid, Fmoc-4-amino-3-methoxybenzoic acid, Fmoc-2-amino-3-methylbenzoic acid, Fmoc-2-amino-5-methylbenzoic acid, Fmoc-2-amino-6-methylbenzoic acid, Fmoc-3-amino-2-methylbenzoic acid, Fmoc-3-amino-4-methylbenzoic acid, Fmoc-4-amino-3-

methylbenzoic acid, Fmoc-3-amino-2-naphtoic acid, Fmoc-D,L-3-amino-3-phenylpropionic acid, Fmoc-L-Methyldopa, Fmoc-2-amino-4,6-dimethyl-3-pyridinecarboxylic acid, Fmoc-D,L-amino-2-thiophenacetic acid, Fmoc-4-(carboxymethyl)piperazine, Fmoc-4-carboxypiperazine, Fmoc-4-(carboxymethyl)homopiperazine, Fmoc-4-phenyl-4-piperidinecarboxylic acid, Fmoc-L-1,2,3,4-tetrahydronorharman-3-carboxylic acid, Fmoc-L-thiazolidine-4-carboxylic acid, all available from The Peptide Laboratory (Richmond, CA, USA).

Non-natural residues can also be added biosynthetically by engineering a suppressor tRNA, typically one that recognizes the UAG stop codon, by chemical aminoacylation with the desired unnatural amino acid. Conventional site-directed mutagenesis is used to introduce the chosen stop codon UAG at the site of interest in the protein gene. When the acylated suppressor tRNA and the mutant gene are combined in an *in vitro* transcription/translation system, the unnatural amino acid is incorporated in response to the UAG codon to give a protein containing that amino acid at the specified position. Liu *et al.*, *Proc. Natl Acad. Sci. USA* 96(9): 4780-5 (1999); Wang *et al.*, *Science* 292(5516): 498-500 (2001).

Fusion Proteins

Another aspect of the present invention relates to the fusion of a polypeptide of the present invention to heterologous polypeptides. In a preferred embodiment, the polypeptide of the present invention is an OSP. In a more preferred embodiment, the polypeptide of the present invention that is fused to a heterologous polypeptide which comprises part or all of the amino acid sequence of SEQ ID NO: 129-295, or is a mutein, homologous polypeptide, analog or derivative thereof. In an even more preferred embodiment, the fusion protein is encoded by a nucleic acid molecule comprising all or part of the nucleic acid sequence of SEQ ID NO: 1-128, or comprises all or part of a nucleic acid sequence that selectively hybridizes or is homologous to a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-128.

The fusion proteins of the present invention will include at least one fragment of a polypeptide of the present invention, which fragment is at least 6, typically at least 8, often at least 15, and usefully at least 16, 17, 18, 19, or 20 amino acids long. The fragment of the polypeptide of the present to be included in the fusion can usefully be at least 25 amino acids long, at least 50 amino acids long, and can be at least 75, 100, or even 150

amino acids long. Fusions that include the entirety of a polypeptide of the present invention have particular utility.

The heterologous polypeptide included within the fusion protein of the present invention is at least 6 amino acids in length, often at least 8 amino acids in length, and preferably at least 15, 20, or 25 amino acids in length. Fusions that include larger polypeptides, such as the IgG Fc region, and even entire proteins (such as GFP chromophore-containing proteins) are particularly useful.

As described above in the description of vectors and expression vectors of the present invention, which discussion is incorporated here by reference in its entirety, heterologous polypeptides to be included in the fusion proteins of the present invention can usefully include those designed to facilitate purification and/or visualization of recombinantly-expressed proteins. *See, e.g.*, Ausubel, Chapter 16, (1992), *supra*. Although purification tags can also be incorporated into fusions that are chemically synthesized, chemical synthesis typically provides sufficient purity that further purification by HPLC suffices; however, visualization tags as above described retain their utility even when the protein is produced by chemical synthesis, and when so included render the fusion proteins of the present invention useful as directly detectable markers of the presence of a polypeptide of the invention.

As also discussed above, heterologous polypeptides to be included in the fusion proteins of the present invention can usefully include those that facilitate secretion of recombinantly expressed proteins into the periplasmic space or extracellular milieu for prokaryotic hosts or into the culture medium for eukaryotic cells through incorporation of secretion signals and/or leader sequences. For example, a His^6 tagged protein can be purified on a Ni affinity column and a GST fusion protein can be purified on a glutathione affinity column. Similarly, a fusion protein comprising the Fc domain of IgG can be purified on a Protein A or Protein G column and a fusion protein comprising an epitope tag such as myc can be purified using an immunoaffinity column containing an anti-c-myc antibody. It is preferable that the epitope tag be separated from the protein encoded by the essential gene by an enzymatic cleavage site that can be cleaved after purification. See also the discussion of nucleic acid molecules encoding fusion proteins that may be expressed on the surface of a cell.

Other useful fusion proteins of the present invention include those that permit use of the polypeptide of the present invention as bait in a yeast two-hybrid system. *See*

Bartel *et al.* (eds.), The Yeast Two-Hybrid System, Oxford University Press (1997); Zhu *et al.*, Yeast Hybrid Technologies, Eaton Publishing (2000); Fields *et al.*, *Trends Genet.* 10(8): 286-92 (1994); Mendelsohn *et al.*, *Curr. Opin. Biotechnol.* 5(5): 482-6 (1994); Luban *et al.*, *Curr. Opin. Biotechnol.* 6(1): 59-64 (1995); Allen *et al.*, *Trends Biochem. Sci.* 20(12): 511-6 (1995); Drees, *Curr. Opin. Chem. Biol.* 3(1): 64-70 (1999); Topcu *et al.*, *Pharm. Res.* 17(9): 1049-55 (2000); Fashena *et al.*, *Gene* 250(1-2): 1-14 (2000); Colas *et al.*, *Nature* 380, 548-550 (1996); Norman, T. *et al.*, *Science* 285, 591-595 (1999); Fabbrizio *et al.*, *Oncogene* 18, 4357-4363 (1999); Xu *et al.*, *Proc Natl Acad Sci U S A.* 94, 12473-12478 (1997); Yang, *et al.*, *Nuc. Acids Res.* 23, 1152-1156 (1995); Kolonin *et al.*, *Proc Natl Acad Sci U S A* 95, 14266-14271 (1998); Cohen *et al.*, *Proc Natl Acad Sci U S A* 95, 14272-14277 (1998); Uetz, *et al. Nature* 403, 623-627(2000); Ito, *et al.*, *Proc Natl Acad Sci U S A* 98, 4569-4574 (2001). Typically, such fusion is to either *E. coli* LexA or yeast GAL4 DNA binding domains. Related bait plasmids are available that express the bait fused to a nuclear localization signal.

Other useful fusion proteins include those that permit display of the encoded polypeptide on the surface of a phage or cell, fusions to intrinsically fluorescent proteins, such as green fluorescent protein (GFP), and fusions to the IgG Fc region, as described above.

The polypeptides of the present invention can also usefully be fused to protein toxins, such as Pseudomonas exotoxin A, diphtheria toxin, shiga toxin A, anthrax toxin lethal factor, or ricin, in order to effect ablation of cells that bind or take up the proteins of the present invention.

Fusion partners include, *inter alia*, *myc*, hemagglutinin (HA), GST, immunoglobulins, β-galactosidase, biotin trpE, protein A, β-lactamase, α-amylase, maltose binding protein, alcohol dehydrogenase, polyhistidine (for example, six histidine at the amino and/or carboxyl terminus of the polypeptide), lacZ, green fluorescent protein (GFP), yeast α mating factor, GAL4 transcription activation or DNA binding domain, luciferase, and serum proteins such as ovalbumin, albumin and the constant domain of IgG. *See, e.g.*, Ausubel (1992), *supra* and Ausubel (1999), *supra*. Fusion proteins may also contain sites for specific enzymatic cleavage, such as a site that is recognized by enzymes such as Factor XIII, trypsin, pepsin, or any other enzyme known in the art. Fusion proteins will typically be made by either recombinant nucleic acid methods, as

described above, chemically synthesized using techniques well known in the art (*e.g.*, a Merrifield synthesis), or produced by chemical cross-linking.

Another advantage of fusion proteins is that the epitope tag can be used to bind the fusion protein to a plate or column through an affinity linkage for screening binding proteins or other molecules that bind to the OSP.

As further described below, the polypeptides of the present invention can readily be used as specific immunogens to raise antibodies that specifically recognize polypeptides of the present invention including OSPs and their allelic variants and homologues. The antibodies, in turn, can be used, *inter alia*, specifically to assay for the polypeptides of the present invention, particularly OSPs, *e.g.* by ELISA for detection of protein fluid samples, such as serum, by immunohistochemistry or laser scanning cytometry, for detection of protein in tissue samples, or by flow cytometry, for detection of intracellular protein in cell suspensions, for specific antibody-mediated isolation and/or purification of OSPs, as for example by immunoprecipitation, and for use as specific agonists or antagonists of OSPs.

One may determine whether polypeptides of the present invention including OSPs, muteins, homologous proteins or allelic variants or fusion proteins of the present invention are functional by methods known in the art. For instance, residues that are tolerant of change while retaining function can be identified by altering the polypeptide at known residues using methods known in the art, such as alanine scanning mutagenesis, Cunningham *et al.*, *Science* 244(4908): 1081-5 (1989); transposon linker scanning mutagenesis, Chen *et al.*, *Gene* 263(1-2): 39-48 (2001); combinations of homolog- and alanine-scanning mutagenesis, Jin *et al.*, *J. Mol. Biol.* 226(3): 851-65 (1992); and combinatorial alanine scanning, Weiss *et al.*, *Proc. Natl. Acad. Sci USA* 97(16): 8950-4 (2000), followed by functional assay. Transposon linker scanning kits are available commercially (New England Biolabs, Beverly, MA, USA, catalog. no. E7-102S; EZ::TN™ In-Frame Linker Insertion Kit, catalogue no. EZI04KN, (Epicentre Technologies Corporation, Madison, WI, USA).

Purification of the polypeptides or fusion proteins of the present invention is well known and within the skill of one having ordinary skill in the art. *See, e.g.*, Scopes, Protein Purification, 2d ed. (1987). Purification of recombinantly expressed polypeptides is described above. Purification of chemically-synthesized peptides can readily be effected, *e.g.*, by HPLC.

Accordingly, it is an aspect of the present invention to provide the isolated polypeptides or fusion proteins of the present invention in pure or substantially pure form in the presence or absence of a stabilizing agent. Stabilizing agents include both proteinaceous and non-proteinaceous material and are well known in the art. Stabilizing agents, such as albumin and polyethylene glycol (PEG) are known and are commercially available.

Although high levels of purity are preferred when the isolated polypeptide or fusion protein of the present invention are used as therapeutic agents, such as in vaccines and replacement therapy, the isolated polypeptides of the present invention are also useful at lower purity. For example, partially purified polypeptides of the present invention can be used as immunogens to raise antibodies in laboratory animals.

In a preferred embodiment, the purified and substantially purified polypeptides of the present invention are in compositions that lack detectable ampholytes, acrylamide monomers, bis-acrylamide monomers, and polyacrylamide.

The polypeptides or fusion proteins of the present invention can usefully be attached to a substrate. The substrate can be porous or solid, planar or non-planar; the bond can be covalent or noncovalent. For example, the peptides of the invention may be stabilized by covalent linkage to albumin. See, U.S. Patent No. 5,876,969, the contents of which are hereby incorporated in its entirety.

The polypeptides or fusion proteins of the present invention can also be usefully bound to a porous substrate, commonly a membrane, typically comprising nitrocellulose, polyvinylidene fluoride (PVDF), or cationically derivatized, hydrophilic PVDF; so bound, the polypeptides or fusion proteins of the present invention can be used to detect and quantify antibodies, *e.g.* in serum, that bind specifically to the immobilized polypeptide or fusion protein of the present invention.

As another example, the polypeptides or fusion proteins of the present invention can usefully be bound to a substantially nonporous substrate, such as plastic, to detect and quantify antibodies, *e.g.* in serum, that bind specifically to the immobilized protein of the present invention. Such plastics include polymethylacrylic, polyethylene, polypropylene, polyacrylate, polymethylmethacrylate, polyvinylchloride, polytetrafluoroethylene, polystyrene, polycarbonate, polyacetal, polysulfone, celluloseacetate, cellulosenitrate, nitrocellulose, or mixtures thereof; when the assay is performed in a standard microtiter dish, the plastic is typically polystyrene.

The polypeptides and fusion proteins of the present invention can also be attached to a substrate suitable for use as a surface enhanced laser desorption ionization source; so attached, the polypeptide or fusion protein of the present invention is useful for binding and then detecting secondary proteins that bind with sufficient affinity or avidity to the surface-bound polypeptide or fusion protein to indicate biologic interaction there between. The polypeptides or fusion proteins of the present invention can also be attached to a substrate suitable for use in surface plasmon resonance detection; so attached, the polypeptide or fusion protein of the present invention is useful for binding and then detecting secondary proteins that bind with sufficient affinity or avidity to the surface-bound polypeptide or fusion protein to indicate biological interaction there between.

Alternative Transcripts

In antother aspect, the present invention provides splice variants of genes and proteins encoded thereby. The identification of a novel splice variant which encodes an amino acid sequence with a novel region can be targeted for the generation of reagents for use in detection and/or treatment of cancer. The novel amino acid sequence may lead to a unique protein structure, protein subcellular localization, biochemical processing or function of the splice variant. This information can be used to directly or indirectly facilitate the generation of additional or novel therapeutics or diagnostics. The nucleotide sequence in this novel splice variant can be used as a nucleic acid probe for the diagnosis and/or treatment of cancer.

Specifically, the newly identified sequences may enable the production of new antibodies or compounds directed against the novel region for use as a therapeutic or diagnostic. Alternatively, the newly identified sequences may alter the biochemical or biological properties of the encoded protein in such a way as to enable the generation of improved or different therapeutics targeting this protein.

Antibodies

In another aspect, the invention provides antibodies, including fragments and derivatives thereof, that bind specifically to polypeptides encoded by the nucleic acid molecules of the invention. In a preferred embodiment, the antibodies are specific for a polypeptide that is an OSP, or a fragment, mutein, derivative, analog or fusion protein thereof. In a more preferred embodiment, the antibodies are specific for a polypeptide that

comprises SEQ ID NO: 129-295, or a fragment, mutein, derivative, analog or fusion protein thereof.

The antibodies of the present invention can be specific for linear epitopes, discontinuous epitopes, or conformational epitopes of such proteins or protein fragments, either as present on the protein in its native conformation or, in some cases, as present on the proteins as denatured, as, *e.g.*, by solubilization in SDS. New epitopes may also be due to a difference in post translational modifications (PTMs) in disease versus normal tissue. For example, a particular site on an OSP may be glycosylated in cancerous cells, but not glycosylated in normal cells or vice versa. In addition, alternative splice forms of an OSP may be indicative of cancer. Differential degradation of the C or N-terminus of an OSP may also be a marker or target for anticancer therapy. For example, an OSP may be N-terminal degraded in cancer cells exposing new epitopes to antibodies which may selectively bind for diagnostic or therapeutic uses.

As is well known in the art, the degree to which an antibody can discriminate among molecular species in a mixture will depend, in part, upon the conformational relatedness of the species in the mixture; typically, the antibodies of the present invention will discriminate over adventitious binding to non-OSP polypeptides by at least two-fold, more typically by at least 5-fold, typically by more than 10-fold, 25-fold, 50-fold, 75-fold, and often by more than 100-fold, and on occasion by more than 500-fold or 1000-fold. When used to detect the proteins or protein fragments of the present invention, the antibody of the present invention is sufficiently specific when it can be used to determine the presence of the polypeptide of the present invention in samples derived from human ovarian.

Typically, the affinity or avidity of an antibody (or antibody multimer, as in the case of an IgM pentamer) of the present invention for a protein or protein fragment of the present invention will be at least about 1 x 10^{-6} molar (M), typically at least about 5 x 10^{-7} M, 1 x 10^{-7} M, with affinities and avidities of at least 1 x 10^{-8} M, 5 x 10^{-9} M, 1 x 10^{-10} M and up to 1 X 10^{-13} M proving especially useful.

The antibodies of the present invention can be naturally occurring forms, such as IgG, IgM, IgD, IgE, IgY, and IgA, from any avian, reptilian, or mammalian species.

Human antibodies can, but will infrequently, be drawn directly from human donors or human cells. In such case, antibodies to the polypeptides of the present invention will typically have resulted from fortuitous immunization, such as autoimmune immunization,

with the polypeptide of the present invention. Such antibodies will typically, but will not invariably, be polyclonal. In addition, individual polyclonal antibodies may be isolated and cloned to generate monoclonals.

Human antibodies are more frequently obtained using transgenic animals that express human immunoglobulin genes, which transgenic animals can be affirmatively immunized with the protein immunogen of the present invention. Human Ig-transgenic mice capable of producing human antibodies and methods of producing human antibodies therefrom upon specific immunization are described, *inter alia*, in U.S. Patent Nos. 6,162,963; 6,150,584; 6,114,598; 6,075,181; 5,939,598; 5,877,397; 5,874,299; 5,814,318; 5,789,650; 5,770,429; 5,661,016; 5,633,425; 5,625,126; 5,569,825; 5,545,807; 5,545,806, and 5,591,669, the disclosures of which are incorporated herein by reference in their entireties. Such antibodies are typically monoclonal, and are typically produced using techniques developed for production of murine antibodies.

Human antibodies are particularly useful, and often preferred, when the antibodies of the present invention are to be administered to human beings as *in vivo* diagnostic or therapeutic agents, since recipient immune response to the administered antibody will often be substantially less than that occasioned by administration of an antibody derived from another species, such as mouse.

IgG, IgM, IgD, IgE, IgY, and IgA antibodies of the present invention are also usefully obtained from other species, including mammals such as rodents (typically mouse, but also rat, guinea pig, and hamster), lagomorphs (typically rabbits), and also larger mammals, such as sheep, goats, cows, and horses; or egg laying birds or reptiles such as chickens or alligators. In such cases, as with the transgenic human-antibody-producing non-human mammals, fortuitous immunization is not required, and the non-human mammal is typically affirmatively immunized, according to standard immunization protocols, with the polypeptide of the present invention. One form of avian antibodies may be generated using techniques described in WO 00/29444, published 25 May 2000, which is herein incorporated by reference in its entirety.

As discussed above, virtually all fragments of 8 or more contiguous amino acids of a polypeptide of the present invention can be used effectively as immunogens when conjugated to a carrier, typically a protein such as bovine thyroglobulin, keyhole limpet hemocyanin, or bovine serum albumin, conveniently using a bifunctional linker such as those described elsewhere above, which discussion is incorporated by reference here.

Immunogenicity can also be conferred by fusion of the polypeptide of the present invention to other moieties. For example, polypeptides of the present invention can be produced by solid phase synthesis on a branched polylysine core matrix; these multiple antigenic peptides (MAPs) provide high purity, increased avidity, accurate chemical definition and improved safety in vaccine development. Tam *et al.*, *Proc. Natl. Acad. Sci. USA* 85: 5409-5413 (1988); Posnett *et al.*, *J. Biol. Chem.* 263: 1719-1725 (1988).

Protocols for immunizing non-human mammals or avian species are well-established in the art. *See* Harlow *et al.* (eds.), Using Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory (1998); Coligan *et al.* (eds.), Current Protocols in Immunology, John Wiley & Sons, Inc. (2001); Zola, Monoclonal Antibodies: Preparation and Use of Monoclonal Antibodies and Engineered Antibody Derivatives (Basics: From Background to Bench), Springer Verlag (2000); Gross M, Speck *J.Dtsch. Tierarztl. Wochenschr.* 103: 417-422 (1996). Immunization protocols often include multiple immunizations, either with or without adjuvants such as Freund's complete adjuvant and Freund's incomplete adjuvant, and may include naked DNA immunization. Moss, *Semin. Immunol.* 2: 317-327 (1990).

Antibodies from non-human mammals and avian species can be polyclonal or monoclonal, with polyclonal antibodies having certain advantages in immunohistochemical detection of the polypeptides of the present invention and monoclonal antibodies having advantages in identifying and distinguishing particular epitopes of the polypeptides of the present invention. Antibodies from avian species may have particular advantage in detection of the polypeptides of the present invention, in human serum or tissues. Vikinge et al., *Biosens. Bioelectron.* 13: 1257-1262 (1998). Following immunization, the antibodies of the present invention can be obtained using any art-accepted technique. Such techniques are well known in the art and are described in detail in references such as Coligan, *supra*; Zola, *supra*; Howard *et al.* (eds.), Basic Methods in Antibody Production and Characterization, CRC Press (2000); Harlow, *supra*; Davis (ed.), Monoclonal Antibody Protocols, Vol. 45, Humana Press (1995); Delves (ed.), Antibody Production: Essential Techniques, John Wiley & Son Ltd (1997); and Kenney, Antibody Solution: An Antibody Methods Manual, Chapman & Hall (1997).

Briefly, such techniques include, *inter alia*, production of monoclonal antibodies by hybridomas and expression of antibodies or fragments or derivatives thereof from host cells engineered to express immunoglobulin genes or fragments thereof. These two

methods of production are not mutually exclusive: genes encoding antibodies specific for the polypeptides of the present invention can be cloned from hybridomas and thereafter expressed in other host cells. Nor need the two necessarily be performed together: *e.g.*, genes encoding antibodies specific for the polypeptides of the present invention can be cloned directly from B cells known to be specific for the desired protein, as further described in U.S. Patent No. 5,627,052, the disclosure of which is incorporated herein by reference in its entirety, or from antibody-displaying phage.

Recombinant expression in host cells is particularly useful when fragments or derivatives of the antibodies of the present invention are desired.

Host cells for recombinant antibody production of whole antibodies, antibody fragments, or antibody derivatives can be prokaryotic or eukaryotic.

Prokaryotic hosts are particularly useful for producing phage displayed antibodies of the present invention.

The technology of phage-displayed antibodies, in which antibody variable region fragments are fused, for example, to the gene III protein (pIII) or gene VIII protein (pVIII) for display on the surface of filamentous phage, such as M13, is by now well-established. *See, e.g.*, Sidhu, *Curr. Opin. Biotechnol.* 11(6): 610-6 (2000); Griffiths *et al.*, *Curr. Opin. Biotechnol.* 9(1): 102-8 (1998); Hoogenboom *et al.*, *Immunotechnology*, 4(1): 1-20 (1998); Rader *et al.*, *Current Opinion in Biotechnology* 8: 503-508 (1997); Aujame *et al.*, *Human Antibodies* 8: 155-168 (1997); Hoogenboom, *Trends in Biotechnol.* 15: 62-70 (1997); de Kruif *et al.*, 17: 453-455 (1996); Barbas *et al.*, *Trends in Biotechnol.* 14: 230-234 (1996); Winter *et al.*, *Ann. Rev. Immunol.* 433-455 (1994). Techniques and protocols required to generate, propagate, screen (pan), and use the antibody fragments from such libraries have recently been compiled. *See, e.g.*, Barbas (2001), *supra*; Kay, *supra*; and Abelson, *supra*.

Typically, phage-displayed antibody fragments are scFv fragments or Fab fragments; when desired, full length antibodies can be produced by cloning the variable regions from the displaying phage into a complete antibody and expressing the full length antibody in a further prokaryotic or a eukaryotic host cell. Eukaryotic cells are also useful for expression of the antibodies, antibody fragments, and antibody derivatives of the present invention. For example, antibody fragments of the present invention can be produced in *Pichia pastoris* and in *Saccharomyces cerevisiae*. *See, e.g.*, Takahashi *et al.*, *Biosci. Biotechnol. Biochem.* 64(10): 2138-44 (2000); Freyre *et al.*, J. Biotechnol. 76(2-3):1 57-63 (2000); Fischer *et al.*, *Biotechnol. Appl. Biochem.* 30 (Pt 2): 117-20

(1999); Pennell *et al.*, *Res. Immunol.* 149(6): 599-603 (1998); Eldin *et al.*, *J. Immunol. Methods.* 201(1): 67-75 (1997);, Frenken *et al.*, *Res. Immunol.* 149(6): 589-99 (1998); and Shusta *et al.*, *Nature Biotechnol.* 16(8): 773-7 (1998).

Antibodies, including antibody fragments and derivatives, of the present invention can also be produced in insect cells. *See, e.g.*, Li *et al.*, *Protein Expr. Purif.* 21(1): 121-8 (2001); Ailor *et al.*, *Biotechnol. Bioeng.* 58(2-3): 196-203 (1998); Hsu *et al.*, *Biotechnol. Prog.* 13(1): 96-104 (1997); Edelman *et al.*, *Immunology* 91(1): 13-9 (1997); and Nesbit *et al.*, *J. Immunol. Methods* 151(1-2): 201-8 (1992).

Antibodies and fragments and derivatives thereof of the present invention can also be produced in plant cells, particularly maize or tobacco, Giddings *et al.*, *Nature Biotechnol.* 18(11): 1151-5 (2000); Gavilondo *et al.*, *Biotechniques* 29(1): 128-38 (2000); Fischer *et al.*, *J. Biol. Regul. Homeost. Agents* 14(2): 83-92 (2000); Fischer *et al.*, *Biotechnol. Appl. Biochem.* 30 (Pt 2): 113-6 (1999); Fischer *et al.*, *Biol. Chem.* 380(7-8): 825-39 (1999); Russell, *Curr. Top. Microbiol. Immunol.* 240: 119-38 (1999); and Ma *et al.*, *Plant Physiol.* 109(2): 341-6 (1995).

Antibodies, including antibody fragments and derivatives, of the present invention can also be produced in transgenic, non-human, mammalian milk. *See, e.g.* Pollock et al., *J. Immunol Methods.* 231: 147-57 (1999); Young et al., *Res. Immunol.* 149: 609-10 (1998); and Limonta et al., *Immunotechnology* 1: 107-13 (1995).

Mammalian cells useful for recombinant expression of antibodies, antibody fragments, and antibody derivatives of the present invention include CHO cells, COS cells, 293 cells, and myeloma cells. Verma *et al.*, *J. Immunol. Methods* 216(1-2):165-81 (1998) review and compare bacterial, yeast, insect and mammalian expression systems for expression of antibodies. Antibodies of the present invention can also be prepared by cell free translation, as further described in Merk *et al.*, *J. Biochem.* (Tokyo) 125(2): 328-33 (1999) and Ryabova *et al.*, *Nature Biotechnol.* 15(1): 79-84 (1997), and in the milk of transgenic animals, as further described in Pollock *et al.*, *J. Immunol. Methods* 231(1-2): 147-57 (1999).

The invention further provides antibody fragments that bind specifically to one or more of the polypeptides of the present invention or to one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention, or the binding of which can be competitively inhibited by one or more of the polypeptides of the present invention or one or more of the polypeptides encoded by the isolated nucleic acid

molecules of the present invention. Among such useful fragments are Fab, Fab', Fv, F(ab)'$_2$, and single-chain Fv (scFv) fragments. Other useful fragments are described in Hudson, *Curr. Opin. Biotechnol.* 9(4): 395-402 (1998).

The present invention also relates to antibody derivatives that bind specifically to one or more of the polypeptides of the present invention, to one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention, or the binding of which can be competitively inhibited by one or more of the polypeptides of the present invention or one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention.

Among such useful derivatives are chimeric, primatized, and humanized antibodies; such derivatives are less immunogenic in human beings, and thus are more suitable for *in vivo* administration, than are unmodified antibodies from non-human mammalian species. Another useful method is PEGylation to increase the serum half life of the antibodies.

Chimeric antibodies typically include heavy and/or light chain variable regions (including both CDR and framework residues) of immunoglobulins of one species, typically mouse, fused to constant regions of another species, typically human. *See, e.g.*, Morrison *et al.*, *Proc. Natl. Acad. Sci USA.*81(21): 6851-5 (1984); Sharon *et al.*, *Nature* 309(5966): 364-7 (1984); Takeda *et al.*, *Nature* 314(6010): 452-4 (1985); and U.S. Patent No. 5,807,715 the disclosure of which is incorporated herein by reference in its entirety. Primatized and humanized antibodies typically include heavy and/or light chain CDRs from a murine antibody grafted into a non-human primate or human antibody V region framework, usually further comprising a human constant region, Riechmann *et al.*, *Nature* 332(6162): 323-7 (1988); Co *et al.*, *Nature* 351(6326): 501-2 (1991); and U.S. Patent Nos. 6,054,297; 5,821,337; 5,770,196; 5,766,886; 5,821,123; 5,869,619; 6,180,377; 6,013,256; 5,693,761; and 6,180,370, the disclosures of which are incorporated herein by reference in their entireties. Other useful antibody derivatives of the invention include heteromeric antibody complexes and antibody fusions, such as diabodies (bispecific antibodies), single-chain diabodies, and intrabodies.

It is contemplated that the nucleic acids encoding the antibodies of the present invention can be operably joined to other nucleic acids forming a recombinant vector for cloning or for expression of the antibodies of the invention. Accordingly, the present invention includes any recombinant vector containing the coding sequences, or part

thereof, whether for eukaryotic transduction, transfection or gene therapy. Such vectors may be prepared using conventional molecular biology techniques, known to those with skill in the art, and would comprise DNA encoding sequences for the immunoglobulin V-regions including framework and CDRs or parts thereof, and a suitable promoter either with or without a signal sequence for intracellular transport. Such vectors may be transduced or transfected into eukaryotic cells or used for gene therapy (Marasco et al., Proc. Natl. Acad. Sci. (USA) 90: 7889-7893 (1993); Duan et al., Proc. Natl. Acad. Sci. (USA) 91: 5075-5079 (1994), by conventional techniques, known to those with skill in the art.

The antibodies of the present invention, including fragments and derivatives thereof, can usefully be labeled. It is, therefore, another aspect of the present invention to provide labeled antibodies that bind specifically to one or more of the polypeptides of the present invention, to one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention, or the binding of which can be competitively inhibited by one or more of the polypeptides of the present invention or one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention. The choice of label depends, in part, upon the desired use.

For example, when the antibodies of the present invention are used for immunohistochemical staining of tissue samples, the label can usefully be an enzyme that catalyzes production and local deposition of a detectable product. Enzymes typically conjugated to antibodies to permit their immunohistochemical visualization are well known, and include alkaline phosphatase, β-galactosidase, glucose oxidase, horseradish peroxidase (HRP), and urease. Typical substrates for production and deposition of visually detectable products include o-nitrophenyl-beta-D-galactopyranoside (ONPG); o-phenylenediamine dihydrochloride (OPD); p-nitrophenyl phosphate (PNPP); p-nitrophenyl-beta-D-galactopryanoside (PNPG); 3',3'-diaminobenzidine (DAB); 3-amino-9-ethylcarbazole (AEC); 4-chloro-1-naphthol (CN); 5-bromo-4-chloro-3-indolyl-phosphate (BCIP); ABTS®; BluoGal; iodonitrotetrazolium (INT); nitroblue tetrazolium chloride (NBT); phenazine methosulfate (PMS); phenolphthalein monophosphate (PMP); tetramethyl benzidine (TMB); tetranitroblue tetrazolium (TNBT); X-Gal; X-Gluc; and X-Glucoside.

Other substrates can be used to produce products for local deposition that are luminescent. For example, in the presence of hydrogen peroxide (H_2O_2), horseradish

peroxidase (HRP) can catalyze the oxidation of cyclic diacylhydrazides, such as luminol. Immediately following the oxidation, the luminol is in an excited state (intermediate reaction product), which decays to the ground state by emitting light. Strong enhancement of the light emission is produced by enhancers, such as phenolic compounds. Advantages include high sensitivity, high resolution, and rapid detection without radioactivity and requiring only small amounts of antibody. *See, e.g.*, Thorpe *et al.*, *Methods Enzymol.* 133: 331-53 (1986); Kricka *et al.*, *J. Immunoassay* 17(1): 67-83 (1996); and Lundqvist *et al.*, *J. Biolumin. Chemilumin.* 10(6): 353-9 (1995). Kits for such enhanced chemiluminescent detection (ECL) are available commercially. The antibodies can also be labeled using colloidal gold.

As another example, when the antibodies of the present invention are used, *e.g.*, for flow cytometric detection, for scanning laser cytometric detection, or for fluorescent immunoassay, they can usefully be labeled with fluorophores. There are a wide variety of fluorophore labels that can usefully be attached to the antibodies of the present invention. For flow cytometric applications, both for extracellular detection and for intracellular detection, common useful fluorophores can be fluorescein isothiocyanate (FITC), allophycocyanin (APC), R-phycoerythrin (PE), peridinin chlorophyll protein (PerCP), Texas Red, Cy3, Cy5, fluorescence resonance energy tandem fluorophores such as PerCP-Cy5.5, PE-Cy5, PE-Cy5.5, PE-Cy7, PE-Texas Red, and APC-Cy7.

Other fluorophores include, *inter alia*, Alexa Fluor® 350, Alexa Fluor® 488, Alexa Fluor® 532, Alexa Fluor® 546, Alexa Fluor® 568, Alexa Fluor® 594, Alexa Fluor® 647 (monoclonal antibody labeling kits available from Molecular Probes, Inc., Eugene, OR, USA), BODIPY dyes, such as BODIPY 493/503, BODIPY FL, BODIPY R6G, BODIPY 530/550, BODIPY TMR, BODIPY 558/568, BODIPY 558/568, BODIPY 564/570, BODIPY 576/589, BODIPY 581/591, BODIPY TR, BODIPY 630/650, BODIPY 650/665, Cascade Blue, Cascade Yellow, Dansyl, lissamine rhodamine B, Marina Blue, Oregon Green 488, Oregon Green 514, Pacific Blue, rhodamine 6G, rhodamine green, rhodamine red, tetramethylrhodamine, Texas Red (available from Molecular Probes, Inc., Eugene, OR, USA), and Cy2, Cy3, Cy3.5, Cy5, Cy5.5, Cy7, all of which are also useful for fluorescently labeling the antibodies of the present invention. For secondary detection using labeled avidin, streptavidin, captavidin or neutravidin, the antibodies of the present invention can usefully be labeled with biotin.

When the antibodies of the present invention are used, *e.g.*, for western blotting applications, they can usefully be labeled with radioisotopes, such as ^{33}P, ^{32}P, ^{35}S, ^{3}H, and ^{125}I. As another example, when the antibodies of the present invention are used for radioimmunotherapy, the label can usefully be ^{228}Th, ^{227}Ac, ^{225}Ac, ^{223}Ra, ^{213}Bi, ^{212}Pb, ^{212}Bi, ^{211}At, ^{203}Pb, ^{194}Os, ^{188}Re, ^{186}Re, ^{153}Sm, ^{149}Tb, ^{131}I, ^{125}I, ^{111}In, ^{105}Rh, ^{99m}Tc, ^{97}Ru, ^{90}Y, ^{90}Sr, ^{88}Y, ^{72}Se, ^{67}Cu, or ^{47}Sc.

As another example, when the antibodies of the present invention are to be used for *in vivo* diagnostic use, they can be rendered detectable by conjugation to MRI contrast agents, such as gadolinium diethylenetriaminepentaacetic acid (DTPA), Lauffer *et al.*, *Radiology* 207(2): 529-38 (1998), or by radioisotopic labeling.

As would be understood, use of the labels described above is not restricted to the application as for which they were mentioned.

The antibodies of the present invention, including fragments and derivatives thereof, can also be conjugated to toxins, in order to target the toxin's ablative action to cells that display and/or express the polypeptides of the present invention. Commonly, the antibody in such immunotoxins is conjugated to Pseudomonas exotoxin A, diphtheria toxin, shiga toxin A, anthrax toxin lethal factor, or ricin. *See* Hall (ed.), Immunotoxin Methods and Protocols (Methods in Molecular Biology, vol. 166), Humana Press (2000); and Frankel *et al.* (eds.), Clinical Applications of Immunotoxins, Springer-Verlag (1998).

The antibodies of the present invention can usefully be attached to a substrate, and it is, therefore, another aspect of the invention to provide antibodies that bind specifically to one or more of the polypeptides of the present invention, to one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention, or the binding of which can be competitively inhibited by one or more of the polypeptides of the present invention or one or more of the polypeptides encoded by the isolated nucleic acid molecules of the present invention, attached to a substrate. Substrates can be porous or nonporous, planar or nonplanar. For example, the antibodies of the present invention can usefully be conjugated to filtration media, such as NHS-activated Sepharose or CNBr-activated Sepharose for purposes of immunoaffinity chromatography. For example, the antibodies of the present invention can usefully be attached to paramagnetic microspheres, typically by biotin-streptavidin interaction, which microsphere can then be used for isolation of cells that express or display the polypeptides of the present invention. As

another example, the antibodies of the present invention can usefully be attached to the surface of a microtiter plate for ELISA.

As noted above, the antibodies of the present invention can be produced in prokaryotic and eukaryotic cells. It is, therefore, another aspect of the present invention to provide cells that express the antibodies of the present invention, including hybridoma cells, B cells, plasma cells, and host cells recombinantly modified to express the antibodies of the present invention.

In yet a further aspect, the present invention provides aptamers evolved to bind specifically to one or more of the OSPs of the present invention or to polypeptides encoded by the OSNAs of the invention.

In sum, one of skill in the art, provided with the teachings of this invention, has available a variety of methods which may be used to alter the biological properties of the antibodies of this invention including methods which would increase or decrease the stability or half-life, immunogenicity, toxicity, affinity or yield of a given antibody molecule, or to alter it in any other way that may render it more suitable for a particular application.

Transgenic Animals and Cells

In another aspect, the invention provides transgenic cells and non-human organisms comprising nucleic acid molecules of the invention. In a preferred embodiment, the transgenic cells and non-human organisms comprise a nucleic acid molecule encoding an OSP. In a preferred embodiment, the OSP comprises an amino acid sequence selected from SEQ ID NO: 129-295, or a fragment, mutein, homologous protein or allelic variant thereof. In another preferred embodiment, the transgenic cells and non-human organism comprise an OSNA of the invention, preferably an OSNA comprising a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-128, or a part, substantially similar nucleic acid molecule, allelic variant or hybridizing nucleic acid molecule thereof.

In another embodiment, the transgenic cells and non-human organisms have a targeted disruption or replacement of the endogenous orthologue of the human OSG. The transgenic cells can be embryonic stem cells or somatic cells. The transgenic non-human organisms can be chimeric, nonchimeric heterozygotes, and nonchimeric homozygotes. Methods of producing transgenic animals are well known in the art. *See*, *e.g.*, Hogan *et*

al., Manipulating the Mouse Embryo: A Laboratory Manual, 2d ed., Cold Spring Harbor Press (1999); Jackson *et al.*, Mouse Genetics and Transgenics: A Practical Approach, Oxford University Press (2000); and Pinkert, Transgenic Animal Technology: A Laboratory Handbook, Academic Press (1999).

Any technique known in the art may be used to introduce a nucleic acid molecule of the invention into an animal to produce the founder lines of transgenic animals. Such techniques include, but are not limited to, pronuclear microinjection. (*see, e.g.*, Paterson *et al.*, *Appl. Microbiol. Biotechnol.* 40: 691-698 (1994); Carver *et al.*, *Biotechnology* 11: 1263-1270 (1993); Wright *et al.*, *Biotechnology* 9: 830-834 (1991); and U.S. Patent No. 4,873,191, herein incorporated by reference in its entirety); retrovirus-mediated gene transfer into germ lines, blastocysts or embryos (*see, e.g.,* Van der Putten *et al.*, *Proc. Natl. Acad. Sci., USA* 82: 6148-6152 (1985)); gene targeting in embryonic stem cells (*see, e.g.,* Thompson *et al.*, *Cell* 56: 313-321 (1989)); electroporation of cells or embryos (*see, e.g.,* Lo, 1983, *Mol. Cell. Biol.* 3: 1803-1814 (1983)); introduction using a gene gun (*see, e.g.*, Ulmer *et al.*, *Science* 259: 1745-49 (1993); introducing nucleic acid constructs into embryonic pleuripotent stem cells and transferring the stem cells back into the blastocyst; and sperm-mediated gene transfer (*see, e.g.,* Lavitrano *et al.*, *Cell* 57: 717-723 (1989)).

Other techniques include, for example, nuclear transfer into enucleated oocytes of nuclei from cultured embryonic, fetal, or adult cells induced to quiescence (*see, e.g.,* Campell *et al.*, *Nature* 380: 64-66 (1996); Wilmut *et al.*, *Nature* 385: 810-813 (1997)). The present invention provides for transgenic animals that carry the transgene (*i.e.*, a nucleic acid molecule of the invention) in all their cells, as well as animals which carry the transgene in some, but not all their cells, i.e. e., mosaic animals or chimeric animals.

The transgene may be integrated as a single transgene or as multiple copies, such as in concatamers, e. g., head-to-head tandems or head-to-tail tandems. The transgene may also be selectively introduced into and activated in a particular cell type by following, *e.g.*, the teaching of Lasko *et al. et al.*, *Proc. Natl. Acad. Sci. USA* 89: 6232- 6236 (1992). The regulatory sequences required for such a cell-type specific activation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art.

Once transgenic animals have been generated, the expression of the recombinant gene may be assayed utilizing standard techniques. Initial screening may be accomplished by Southern blot analysis or PCR techniques to analyze animal tissues to verify that integration of the transgene has taken place. The level of mRNA expression of the

transgene in the tissues of the transgenic animals may also be assessed using techniques which include, but are not limited to, Northern blot analysis of tissue samples obtained from the animal, in situ hybridization analysis, and reverse transcriptase-PCR (RT-PCR). Samples of transgenic gene-expressing tissue may also be evaluated immunocytochemically or immunohistochemically using antibodies specific for the transgene product.

Once the founder animals are produced, they may be bred, inbred, outbred, or crossbred to produce colonies of the particular animal. Examples of such breeding strategies include, but are not limited to: outbreeding of founder animals with more than one integration site in order to establish separate lines; inbreeding of separate lines in order to produce compound transgenics that express the transgene at higher levels because of the effects of additive expression of each transgene; crossing of heterozygous transgenic animals to produce animals homozygous for a given integration site in order to both augment expression and eliminate the need for screening of animals by DNA analysis; crossing of separate homozygous lines to produce compound heterozygous or homozygous lines; and breeding to place the transgene on a distinct background that is appropriate for an experimental model of interest.

Transgenic animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

Methods for creating a transgenic animal with a disruption of a targeted gene are also well known in the art. In general, a vector is designed to comprise some nucleotide sequences homologous to the endogenous targeted gene. The vector is introduced into a cell so that it may integrate, via homologous recombination with chromosomal sequences, into the endogenous gene, thereby disrupting the function of the endogenous gene. The transgene may also be selectively introduced into a particular cell type, thus inactivating the endogenous gene in only that cell type. *See, e.g.,* Gu *et al.*, *Science* 265: 103-106 (1994). The regulatory sequences required for such a cell-type specific inactivation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art. *See, e.g.*, Smithies *et al.*, *Nature* 317: 230-234 (1985); Thomas *et al., Cell* 51: 503-512 (1987); Thompson *et al.*, *Cell* 5: 313-321 (1989).

In one embodiment, a mutant, non-functional nucleic acid molecule of the invention (or a completely unrelated DNA sequence) flanked by DNA homologous to the endogenous nucleic acid sequence (either the coding regions or regulatory regions of the gene) can be used, with or without a selectable marker and/or a negative selectable marker, to transfect cells that express polypeptides of the invention in vivo. In another embodiment, techniques known in the art are used to generate knockouts in cells that contain, but do not express the gene of interest. Insertion of the DNA construct, via targeted homologous recombination, results in inactivation of the targeted gene. Such approaches are particularly suited in research and agricultural fields where modifications to embryonic stem cells can be used to generate animal offspring with an inactive targeted gene. *See, e.g.,* Thomas, *supra* and Thompson, *supra*. However this approach can be routinely adapted for use in humans provided the recombinant DNA constructs are directly administered or targeted to the required site in vivo using appropriate viral vectors that will be apparent to those of skill in the art.

In further embodiments of the invention, cells that are genetically engineered to express the polypeptides of the invention, or alternatively, that are genetically engineered not to express the polypeptides of the invention (*e.g.*, knockouts) are administered to a patient in vivo. Such cells may be obtained from an animal or patient or an MHC compatible donor and can include, but are not limited to fibroblasts, bone marrow cells, blood cells (*e.g.*, lymphocytes), adipocytes, muscle cells, endothelial cells etc. The cells are genetically engineered in vitro using recombinant DNA techniques to introduce the coding sequence of polypeptides of the invention into the cells, or alternatively, to disrupt the coding sequence and/or endogenous regulatory sequence associated with the polypeptides of the invention, *e.g.*, by transduction (using viral vectors, and preferably vectors that integrate the transgene into the cell genome) or transfection procedures, including, but not limited to, the use of plasmids, cosmids, YACs, naked DNA, electroporation, liposomes, etc.

The coding sequence of the polypeptides of the invention can be placed under the control of a strong constitutive or inducible promoter or promoter/enhancer to achieve expression, and preferably secretion, of the polypeptides of the invention. The engineered cells which express and preferably secrete the polypeptides of the invention can be introduced into the patient systemically, *e.g.*, in the circulation, or intraperitoneally.

Alternatively, the cells can be incorporated into a matrix and implanted in the body, *e.g.*, genetically engineered fibroblasts can be implanted as part of a skin graft; genetically engineered endothelial cells can be implanted as part of a lymphatic or vascular graft. *See, e.g.,* U.S. Patent Nos. 5,399,349 and 5,460,959, each of which is incorporated by reference herein in its entirety.

When the cells to be administered are non-autologous or non-MHC compatible cells, they can be administered using well known techniques which prevent the development of a host immune response against the introduced cells. For example, the cells may be introduced in an encapsulated form which, while allowing for an exchange of components with the immediate extracellular environment, does not allow the introduced cells to be recognized by the host immune system.

Transgenic and "knock-out" animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

Computer Readable Means

A further aspect of the invention is a computer readable means for storing the nucleic acid and amino acid sequences of the instant invention. In a preferred embodiment, the invention provides a computer readable means for storing SEQ ID NO: 129-295 and SEQ ID NO: 1-128 as described herein, as the complete set of sequences or in any combination. The records of the computer readable means can be accessed for reading and display and for interface with a computer system for the application of programs allowing for the location of data upon a query for data meeting certain criteria, the comparison of sequences, the alignment or ordering of sequences meeting a set of criteria, and the like.

The nucleic acid and amino acid sequences of the invention are particularly useful as components in databases useful for search analyses as well as in sequence analysis algorithms. As used herein, the terms "nucleic acid sequences of the invention" and "amino acid sequences of the invention" mean any detectable chemical or physical characteristic of a polynucleotide or polypeptide of the invention that is or may be reduced to or stored in a computer readable form. These include, without limitation,

chromatographic scan data or peak data, photographic data or scan data therefrom, and mass spectrographic data.

This invention provides computer readable media having stored thereon sequences of the invention. A computer readable medium may comprise one or more of the following: a nucleic acid sequence comprising a sequence of a nucleic acid sequence of the invention; an amino acid sequence comprising an amino acid sequence of the invention; a set of nucleic acid sequences wherein at least one of said sequences comprises the sequence of a nucleic acid sequence of the invention; a set of amino acid sequences wherein at least one of said sequences comprises the sequence of an amino acid sequence of the invention; a data set representing a nucleic acid sequence comprising the sequence of one or more nucleic acid sequences of the invention; a data set representing a nucleic acid sequence encoding an amino acid sequence comprising the sequence of an amino acid sequence of the invention; a set of nucleic acid sequences wherein at least one of said sequences comprises the sequence of a nucleic acid sequence of the invention; a set of amino acid sequences wherein at least one of said sequences comprises the sequence of an amino acid sequence of the invention; a data set representing a nucleic acid sequence comprising the sequence of a nucleic acid sequence of the invention; a data set representing a nucleic acid sequence encoding an amino acid sequence comprising the sequence of an amino acid sequence of the invention. The computer readable medium can be any composition of matter used to store information or data, including, for example, commercially available floppy disks, tapes, hard drives, compact disks, and video disks.

Also provided by the invention are methods for the analysis of character sequences, particularly genetic sequences. Preferred methods of sequence analysis include, for example, methods of sequence homology analysis, such as identity and similarity analysis, RNA structure analysis, sequence assembly, cladistic analysis, sequence motif analysis, open reading frame determination, nucleic acid base calling, and sequencing chromatogram peak analysis.

A computer-based method is provided for performing nucleic acid sequence identity or similarity identification. This method comprises the steps of providing a nucleic acid sequence comprising the sequence of a nucleic acid of the invention in a computer readable medium; and comparing said nucleic acid sequence to at least one nucleic acid or amino acid sequence to identify sequence identity or similarity.

A computer-based method is also provided for performing amino acid homology identification, said method comprising the steps of: providing an amino acid sequence comprising the sequence of an amino acid of the invention in a computer readable medium; and comparing said amino acid sequence to at least one nucleic acid or an amino acid sequence to identify homology.

A computer-based method is still further provided for assembly of overlapping nucleic acid sequences into a single nucleic acid sequence, said method comprising the steps of: providing a first nucleic acid sequence comprising the sequence of a nucleic acid of the invention in a computer readable medium; and screening for at least one overlapping region between said first nucleic acid sequence and a second nucleic acid sequence. In addition, the invention includes a method of using patterns of expression associated with either the nucleic acids or proteins in a computer-based method to diagnose disease.

Diagnostic Methods for Ovarian Cancer

The present invention also relates to quantitative and qualitative diagnostic assays and methods for detecting, diagnosing, monitoring, staging and predicting cancers by comparing expression of an OSNA or an OSP in a human patient that has or may have ovarian cancer, or who is at risk of developing ovarian cancer, with the expression of an OSNA or an OSP in a normal human control. For purposes of the present invention, "expression of an OSNA" or "OSNA expression" means the quantity of OSNA mRNA that can be measured by any method known in the art or the level of transcription that can be measured by any method known in the art in a cell, tissue, organ or whole patient. Similarly, the term "expression of an OSP" or "OSP expression" means the amount of OSP that can be measured by any method known in the art or the level of translation of an OSNA that can be measured by any method known in the art.

The present invention provides methods for diagnosing ovarian cancer in a patient, by analyzing for changes in levels of OSNA or OSP in cells, tissues, organs or bodily fluids compared with levels of OSNA or OSP in cells, tissues, organs or bodily fluids of preferably the same type from a normal human control, wherein an increase, or decrease in certain cases, in levels of an OSNA or OSP in the patient versus the normal human control is associated with the presence of ovarian cancer or with a predilection to the disease. In another preferred embodiment, the present invention provides methods for diagnosing

ovarian cancer in a patient by analyzing changes in the structure of the mRNA of an OSG compared to the mRNA from a normal control. These changes include, without limitation, aberrant splicing, alterations in polyadenylation and/or alterations in 5' nucleotide capping. In yet another preferred embodiment, the present invention provides methods for diagnosing ovarian cancer in a patient by analyzing changes in an OSP compared to an OSP from a normal patient. These changes include, *e.g.*, alterations, including post translational modifications such as glycosylation and/or phosphorylation of the OSP or changes in the subcellular OSP localization.

For purposes of the present invention, diagnosing means that OSNA or OSP levels are used to determine the presence or absence of disease in a patient. As will be understood by those of skill in the art, measurement of other diagnostic parameters may be required for definitive diagnosis or determination of the appropriate treatment for the disease. The determination may be made by a clinician, a doctor, a testing laboratory, or a patient using an over the counter test. The patient may have symptoms of disease or may be asymptomatic. In addition, the OSNA or OSP levels of the present invention may be used as screening marker to determine whether further tests or biopsies are warranted. In addition, the OSNA or OSP levels may be used to determine the vulnerability or susceptibility to disease.

In a preferred embodiment, the expression of an OSNA is measured by determining the amount of a mRNA that encodes an amino acid sequence selected from SEQ ID NO: 129-295, a homolog, an allelic variant, or a fragment thereof. In a more preferred embodiment, the OSNA expression that is measured is the level of expression of an OSNA mRNA selected from SEQ ID NO: 1-128, or a hybridizing nucleic acid, homologous nucleic acid or allelic variant thereof, or a part of any of these nucleic acid molecules. OSNA expression may be measured by any method known in the art, such as those described *supra*, including measuring mRNA expression by Northern blot, quantitative or qualitative reverse transcriptase PCR (RT-PCR), microarray, dot or slot blots or *in situ* hybridization. *See, e.g.*, Ausubel (1992), *supra*; Ausubel (1999), *supra*; Sambrook (1989), *supra*; and Sambrook (2001), *supra*. OSNA transcription may be measured by any method known in the art including using a reporter gene hooked up to the promoter of an OSG of interest or doing nuclear run-off assays. Alterations in mRNA structure, *e.g.*, aberrant splicing variants, may be determined by any method known in the art, including, RT-PCR followed by sequencing or restriction analysis. As necessary,

OSNA expression may be compared to a known control, such as normal ovarian nucleic acid, to detect a change in expression.

In another preferred embodiment, the expression of an OSP is measured by determining the level of an OSP having an amino acid sequence selected from the group consisting of SEQ ID NO: 129-295, a homolog, an allelic variant, or a fragment thereof. Such levels are preferably determined in at least one of cells, tissues, organs and/or bodily fluids, including determination of normal and abnormal levels. Thus, for instance, a diagnostic assay in accordance with the invention for diagnosing over- or underexpression of an OSNA or OSP compared to normal control bodily fluids, cells, or tissue samples may be used to diagnose the presence of ovarian cancer. The expression level of an OSP may be determined by any method known in the art, such as those described *supra*. In a preferred embodiment, the OSP expression level may be determined by radioimmunoassays, competitive-binding assays, ELISA, Western blot, FACS, immunohistochemistry, immunoprecipitation, proteomic approaches: two-dimensional gel electrophoresis (2D electrophoresis) and non-gel-based approaches such as mass spectrometry or protein interaction profiling. *See*, e.g, Harlow (1999), *supra*; Ausubel (1992), *supra*; and Ausubel (1999), *supra*. Alterations in the OSP structure may be determined by any method known in the art, including, *e.g.*, using antibodies that specifically recognize phosphoserine, phosphothreonine or phosphotyrosine residues, two-dimensional polyacrylamide gel electrophoresis (2D PAGE) and/or chemical analysis of amino acid residues of the protein. *Id.*

In a preferred embodiment, a radioimmunoassay (RIA) or an ELISA is used. An antibody specific to an OSP is prepared if one is not already available. In a preferred embodiment, the antibody is a monoclonal antibody. The anti-OSP antibody is bound to a solid support and any free protein binding sites on the solid support are blocked with a protein such as bovine serum albumin. A sample of interest is incubated with the antibody on the solid support under conditions in which the OSP will bind to the anti-OSP antibody. The sample is removed, the solid support is washed to remove unbound material, and an anti-OSP antibody that is linked to a detectable reagent (a radioactive substance for RIA and an enzyme for ELISA) is added to the solid support and incubated under conditions in which binding of the OSP to the labeled antibody will occur. After binding, the unbound labeled antibody is removed by washing. For an ELISA, one or more substrates are added to produce a colored reaction product that is based upon the amount of an OSP in the

sample. For an RIA, the solid support is counted for radioactive decay signals by any method known in the art. Quantitative results for both RIA and ELISA typically are obtained by reference to a standard curve.

Other methods to measure OSP levels are known in the art. For instance, a competition assay may be employed wherein an anti-OSP antibody is attached to a solid support and an allocated amount of a labeled OSP and a sample of interest are incubated with the solid support. The amount of labeled OSP attached to the solid support can be correlated to the quantity of an OSP in the sample.

Of the proteomic approaches, 2D PAGE is a well known technique. Isolation of individual proteins from a sample such as serum is accomplished using sequential separation of proteins by isoelectric point and molecular weight. Typically, polypeptides are first separated by isoelectric point (the first dimension) and then separated by size using an electric current (the second dimension). In general, the second dimension is perpendicular to the first dimension. Because no two proteins with different sequences are identical on the basis of both size and charge, the result of 2D PAGE is a roughly square gel in which each protein occupies a unique spot. Analysis of the spots with chemical or antibody probes, or subsequent protein microsequencing can reveal the relative abundance of a given protein and the identity of the proteins in the sample.

Expression levels of an OSNA can be determined by any method known in the art, including PCR and other nucleic acid methods, such as ligase chain reaction (LCR) and nucleic acid sequence based amplification (NASBA), can be used to detect malignant cells for diagnosis and monitoring of various malignancies. For example, reverse-transcriptase PCR (RT-PCR) is a powerful technique which can be used to detect the presence of a specific mRNA population in a complex mixture of thousands of other mRNA species. In RT-PCR, an mRNA species is first reverse transcribed to complementary DNA (cDNA) with use of the enzyme reverse transcriptase; the cDNA is then amplified as in a standard PCR reaction.

Hybridization to specific DNA molecules (*e.g.*, oligonucleotides) arrayed on a solid support can be used to both detect the expression of and quantitate the level of expression of one or more OSNAs of interest. In this approach, all or a portion of one or more OSNAs is fixed to a substrate. A sample of interest, which may comprise RNA, *e.g.*, total RNA or polyA-selected mRNA, or a complementary DNA (cDNA) copy of the RNA is incubated with the solid support under conditions in which hybridization will occur

between the DNA on the solid support and the nucleic acid molecules in the sample of interest. Hybridization between the substrate-bound DNA and the nucleic acid molecules in the sample can be detected and quantitated by several means, including, without limitation, radioactive labeling or fluorescent labeling of the nucleic acid molecule or a secondary molecule designed to detect the hybrid.

The above tests can be carried out on samples derived from a variety of cells, bodily fluids and/or tissue extracts such as homogenates or solubilized tissue obtained from a patient. Tissue extracts are obtained routinely from tissue biopsy and autopsy material. Bodily fluids useful in the present invention include blood, urine, saliva or any other bodily secretion or derivative thereof. As used herein "blood" includes whole blood, plasma, serum, circulating epithelial cells, constituents, or any derivative of blood.

In addition to detection in bodily fluids, the proteins and nucleic acids of the invention are suitable to detection by cell capture technology. Whole cells may be captured by a variety methods for example magnetic separation, such as described in U.S. Patent. Nos. 5,200,084; 5,186,827; 5,108,933; and 4,925,788, the disclosures of which are incorporated herein by reference in their entireties. Epithelial cells may be captured using such products as Dynabeads® or CELLection™ (Dynal Biotech, Oslo, Norway). Alternatively, fractions of blood may be captured, e.g., the buffy coat fraction (50mm cells isolated from 5ml of blood) containing epithelial cells. In addition, cancer cells may be captured using the techniques described in WO 00/47998, the disclosure of which is incorporated herein by reference in its entirety. Once the cells are captured or concentrated, the proteins or nucleic acids are detected by the means described in the subject application. Alternatively, nucleic acids may be captured directly from blood samples, see U.S. Patent Nos. 6,156,504, 5,501,963; or WO 01/42504, the disclosures of which are incorporated herein by reference in their entireties.

In a preferred embodiment, the specimen tested for expression of OSNA or OSP includes without limitation ovarian tissue, ovarian cells grown in cell culture, blood, serum, lymph node tissue, and lymphatic fluid. In another preferred embodiment, especially when metastasis of a primary ovarian cancer is known or suspected, specimens include, without limitation, tissues from brain, bone, bone marrow, liver, lungs, colon, and adrenal glands. In general, the tissues may be sampled by biopsy, including, without limitation, needle biopsy, *e.g.*, transthoracic needle aspiration, cervical mediatinoscopy,

endoscopic lymph node biopsy, video-assisted thoracoscopy, exploratory thoracotomy, bone marrow biopsy and bone marrow aspiration.

All the methods of the present invention may optionally include determining the expression levels of one or more other cancer markers in addition to determining the expression level of an OSNA or OSP. In many cases, the use of another cancer marker will decrease the likelihood of false positives or false negatives. In one embodiment, the one or more other cancer markers include other OSNAs or OSPs as disclosed herein. Other cancer markers useful in the present invention will depend on the cancer being tested and are known to those of skill in the art. In a preferred embodiment, at least one other cancer marker in addition to a particular OSNA or OSP is measured. In a more preferred embodiment, at least two other additional cancer markers are used. In an even more preferred embodiment, at least three, more preferably at least five, even more preferably at least ten additional cancer markers are used.

Diagnosing

In one aspect, the invention provides a method for determining the expression levels and/or structural alterations of one or more OSNA and/or OSP in a sample from a patient suspected of having ovarian cancer. In general, the method comprises the steps of obtaining the sample from the patient, determining the expression level or structural alterations of an OSNA and/or OSP and then ascertaining whether the patient has ovarian cancer from the expression level of the OSNA or OSP. In general, if high expression relative to a control of an OSNA or OSP is indicative of ovarian cancer, a diagnostic assay is considered positive if the level of expression of the OSNA or OSP is at least one and a half times higher, and more preferably are at least two times higher, still more preferably five times higher, even more preferably at least ten times higher, than in preferably the same cells, tissues or bodily fluid of a normal human control. In contrast, if low expression relative to a control of an OSNA or OSP is indicative of ovarian cancer, a diagnostic assay is considered positive if the level of expression of the OSNA or OSP is at least one and a half times lower, and more preferably are at least two times lower, still more preferably five times lower, even more preferably at least ten times lower than in preferably the same cells, tissues or bodily fluid of a normal human control. The normal human control may be from a different patient or from uninvolved tissue of the same patient.

The present invention also provides a method of determining whether ovarian cancer has metastasized in a patient. One may identify whether the ovarian cancer has metastasized by measuring the expression levels and/or structural alterations of one or more OSNAs and/or OSPs in a variety of tissues. The presence of an OSNA or OSP in a tissue other than ovarian at levels higher than that of corresponding noncancerous tissue (*e.g.*, the same tissue from another individual) is indicative of metastasis if high level expression of an OSNA or OSP is associated with ovarian cancer. Similarly, the presence of an OSNA or OSP in a tissue other than ovarian at levels lower than that of corresponding noncancerous tissue is indicative of metastasis if low level expression of an OSNA or OSP is associated with ovarian cancer. Further, the presence of a structurally altered OSNA or OSP that is associated with ovarian cancer is also indicative of metastasis.

In general, if high expression relative to a control of an OSNA or OSP is indicative of metastasis, an assay for metastasis is considered positive if the level of expression of the OSNA or OSP is at least one and a half times higher, and more preferably are at least two times higher, still more preferably five times higher, even more preferably at least ten times higher, than in preferably the same cells, tissues or bodily fluid of a normal human control. In contrast, if low expression relative to a control of an OSNA or OSP is indicative of metastasis, an assay for metastasis is considered positive if the level of expression of the OSNA or OSP is at least one and a half times lower, and more preferably are at least two times lower, still more preferably five times lower, even more preferably at least ten times lower than in preferably the same cells, tissues or bodily fluid of a normal human control.

Staging

The invention also provides a method of staging ovarian cancer in a human patient. The method comprises identifying a human patient having ovarian cancer and analyzing cells, tissues or bodily fluids from such human patient for expression levels and/or structural alterations of one or more OSNAs or OSPs. First, one or more tumors from a variety of patients are staged according to procedures well known in the art, and the expression levels of one or more OSNAs or OSPs is determined for each stage to obtain a standard expression level for each OSNA and OSP. Then, the OSNA or OSP expression

levels of the OSNA or OSP are determined in a biological sample from a patient whose stage of cancer is not known. The OSNA or OSP expression levels from the patient are then compared to the standard expression level. By comparing the expression level of the OSNAs and OSPs from the patient to the standard expression levels, one may determine the stage of the tumor. The same procedure may be followed using structural alterations of an OSNA or OSP to determine the stage of a ovarian cancer.

Monitoring

Further provided is a method of monitoring ovarian cancer in a human patient. One may monitor a human patient to determine whether there has been metastasis and, if there has been, when metastasis began to occur. One may also monitor a human patient to determine whether a preneoplastic lesion has become cancerous. One may also monitor a human patient to determine whether a therapy, *e.g.*, chemotherapy, radiotherapy or surgery, has decreased or eliminated the ovarian cancer. The monitoring may determine if there has been a reoccurrence and, if so, determine its nature. The method comprises identifying a human patient that one wants to monitor for ovarian cancer, periodically analyzing cells, tissues or bodily fluids from such human patient for expression levels of one or more OSNAs or OSPs, and comparing the OSNA or OSP levels over time to those OSNA or OSP expression levels obtained previously. Patients may also be monitored by measuring one or more structural alterations in an OSNA or OSP that are associated with ovarian cancer.

If increased expression of an OSNA or OSP is associated with metastasis, treatment failure, or conversion of a preneoplastic lesion to a cancerous lesion, then detecting an increase in the expression level of an OSNA or OSP indicates that the tumor is metastasizing, that treatment has failed or that the lesion is cancerous, respectively. One having ordinary skill in the art would recognize that if this were the case, then a decreased expression level would be indicative of no metastasis, effective therapy or failure to progress to a neoplastic lesion. If decreased expression of an OSNA or OSP is associated with metastasis, treatment failure, or conversion of a preneoplastic lesion to a cancerous lesion, then detecting a decrease in the expression level of an OSNA or OSP indicates that the tumor is metastasizing, that treatment has failed or that the lesion is cancerous, respectively. In a preferred embodiment, the levels of OSNAs or OSPs are determined from the same cell type, tissue or bodily fluid as prior patient samples. Monitoring a

patient for onset of ovarian cancer metastasis is periodic and preferably is done on a quarterly basis, but may be done more or less frequently.

The methods described herein can further be utilized as prognostic assays to identify subjects having or at risk of developing a disease or disorder associated with increased or decreased expression levels of an OSNA and/or OSP. The present invention provides a method in which a test sample is obtained from a human patient and one or more OSNAs and/or OSPs are detected. The presence of higher (or lower) OSNA or OSP levels as compared to normal human controls is diagnostic for the human patient being at risk for developing cancer, particularly ovarian cancer. The effectiveness of therapeutic agents to decrease (or increase) expression or activity of one or more OSNAs and/or OSPs of the invention can also be monitored by analyzing levels of expression of the OSNAs and/or OSPs in a human patient in clinical trials or in *in vitro* screening assays such as in human cells. In this way, the gene expression pattern can serve as a marker, indicative of the physiological response of the human patient or cells, as the case may be, to the agent being tested.

Detection of Genetic Lesions or Mutations

The methods of the present invention can also be used to detect genetic lesions or mutations in an OSG, thereby determining if a human with the genetic lesion is susceptible to developing ovarian cancer or to determine what genetic lesions are responsible, or are partly responsible, for a person's existing ovarian cancer. Genetic lesions can be detected, for example, by ascertaining the existence of a deletion, insertion and/or substitution of one or more nucleotides from the OSGs of this invention, a chromosomal rearrangement of an OSG, an aberrant modification of an OSG (such as of the methylation pattern of the genomic DNA), or allelic loss of an OSG. Methods to detect such lesions in the OSG of this invention are known to those having ordinary skill in the art following the teachings of the specification.

Methods of Detecting Noncancerous Ovarian Diseases

The present invention also provides methods for determining the expression levels and/or structural alterations of one or more OSNAs and/or OSPs in a sample from a patient suspected of having or known to have a noncancerous ovarian disease. In general, the method comprises the steps of obtaining a sample from the patient, determining the expression level or structural alterations of an OSNA and/or OSP, comparing the

expression level or structural alteration of the OSNA or OSP to a normal ovarian control, and then ascertaining whether the patient has a noncancerous ovarian disease. In general, if high expression relative to a control of an OSNA or OSP is indicative of a particular noncancerous ovarian disease, a diagnostic assay is considered positive if the level of expression of the OSNA or OSP is at least two times higher, and more preferably are at least five times higher, even more preferably at least ten times higher, than in preferably the same cells, tissues or bodily fluid of a normal human control. In contrast, if low expression relative to a control of an OSNA or OSP is indicative of a noncancerous ovarian disease, a diagnostic assay is considered positive if the level of expression of the OSNA or OSP is at least two times lower, more preferably are at least five times lower, even more preferably at least ten times lower than in preferably the same cells, tissues or bodily fluid of a normal human control. The normal human control may be from a different patient or from uninvolved tissue of the same patient.

One having ordinary skill in the art may determine whether an OSNA and/or OSP is associated with a particular noncancerous ovarian disease by obtaining ovarian tissue from a patient having a noncancerous ovarian disease of interest and determining which OSNAs and/or OSPs are expressed in the tissue at either a higher or a lower level than in normal ovarian tissue. In another embodiment, one may determine whether an OSNA or OSP exhibits structural alterations in a particular noncancerous ovarian disease state by obtaining ovarian tissue from a patient having a noncancerous ovarian disease of interest and determining the structural alterations in one or more OSNAs and/or OSPs relative to normal ovarian tissue.

Methods for Identifying Ovarian Tissue

In another aspect, the invention provides methods for identifying ovarian tissue. These methods are particularly useful in, *e.g.*, forensic science, ovarian cell differentiation and development, and in tissue engineering.

In one embodiment, the invention provides a method for determining whether a sample is ovarian tissue or has ovarian tissue-like characteristics. The method comprises the steps of providing a sample suspected of comprising ovarian tissue or having ovarian tissue-like characteristics, determining whether the sample expresses one or more OSNAs and/or OSPs, and, if the sample expresses one or more OSNAs and/or OSPs, concluding that the sample comprises ovarian tissue. In a preferred embodiment, the OSNA encodes

a polypeptide having an amino acid sequence selected from SEQ ID NO: 129-295, or a homolog, allelic variant or fragment thereof. In a more preferred embodiment, the OSNA has a nucleotide sequence selected from SEQ ID NO: 1-128, or a hybridizing nucleic acid, an allelic variant or a part thereof. Determining whether a sample expresses an OSNA can be accomplished by any method known in the art. Preferred methods include hybridization to microarrays, Northern blot hybridization, and quantitative or qualitative RT-PCR. In another preferred embodiment, the method can be practiced by determining whether an OSP is expressed. Determining whether a sample expresses an OSP can be accomplished by any method known in the art. Preferred methods include Western blot, ELISA, RIA and 2D PAGE. In one embodiment, the OSP has an amino acid sequence selected from SEQ ID NO: 129-295, or a homolog, allelic variant or fragment thereof. In another preferred embodiment, the expression of at least two OSNAs and/or OSPs is determined. In a more preferred embodiment, the expression of at least three, more preferably four and even more preferably five OSNAs and/or OSPs are determined.

In one embodiment, the method can be used to determine whether an unknown tissue is ovarian tissue. This is particularly useful in forensic science, in which small, damaged pieces of tissues that are not identifiable by microscopic or other means are recovered from a crime or accident scene. In another embodiment, the method can be used to determine whether a tissue is differentiating or developing into ovarian tissue. This is important in monitoring the effects of the addition of various agents to cell or tissue culture, *e.g.*, in producing new ovarian tissue by tissue engineering. These agents include, *e.g.*, growth and differentiation factors, extracellular matrix proteins and culture medium. Other factors that may be measured for effects on tissue development and differentiation include gene transfer into the cells or tissues, alterations in pH, aqueous:air interface and various other culture conditions.

Methods for Producing and Modifying Ovarian Tissue

In another aspect, the invention provides methods for producing engineered ovarian tissue or cells. In one embodiment, the method comprises the steps of providing cells, introducing an OSNA or an OSG into the cells, and growing the cells under conditions in which they exhibit one or more properties of ovarian tissue cells. In a preferred embodiment, the cells are pleuripotent. As is well known in the art, normal ovarian tissue comprises a large number of different cell types. Thus, in one embodiment,

the engineered ovarian tissue or cells comprises one of these cell types. In another embodiment, the engineered ovarian tissue or cells comprises more than one ovarian cell type. Further, the culture conditions of the cells or tissue may require manipulation in order to achieve full differentiation and development of the ovarian cell tissue. Methods for manipulating culture conditions are well known in the art.

Nucleic acid molecules encoding one or more OSPs are introduced into cells, preferably pleuripotent cells. In a preferred embodiment, the nucleic acid molecules encode OSPs having amino acid sequences selected from SEQ ID NO: 129-295, or homologous proteins, analogs, allelic variants or fragments thereof. In a more preferred embodiment, the nucleic acid molecules have a nucleotide sequence selected from SEQ ID NO: 1-128, or hybridizing nucleic acids, allelic variants or parts thereof. In another highly preferred embodiment, an OSG is introduced into the cells. Expression vectors and methods of introducing nucleic acid molecules into cells are well known in the art and are described in detail, *supra*.

Artificial ovarian tissue may be used to treat patients who have lost some or all of their ovarian function.

Pharmaceutical Compositions

In another aspect, the invention provides pharmaceutical compositions comprising the nucleic acid molecules, polypeptides, fusion proteins, antibodies, antibody derivatives, antibody fragments, agonists, antagonists, or inhibitors of the present invention. In a preferred embodiment, the pharmaceutical composition comprises an OSNA or part thereof. In a more preferred embodiment, the OSNA has a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-128, a nucleic acid that hybridizes thereto, an allelic variant thereof, or a nucleic acid that has substantial sequence identity thereto. In another preferred embodiment, the pharmaceutical composition comprises an OSP or fragment thereof. In a more preferred embodiment, the pharmaceutical composition comprises an OSP having an amino acid sequence that is selected from the group consisting of SEQ ID NO: 129-295, a polypeptide that is homologous thereto, a fusion protein comprising all or a portion of the polypeptide, or an analog or derivative thereof. In another preferred embodiment, the pharmaceutical composition comprises an anti-OSP antibody, preferably an antibody that specifically binds to an OSP having an amino acid that is selected from the group consisting of SEQ ID NO: 129-295, or an antibody that

binds to a polypeptide that is homologous thereto, a fusion protein comprising all or a portion of the polypeptide, or an analog or derivative thereof.

Due to the association of angiogenesis with cancer vascularization there is great need of new markers and methods for diagnosing angiogenesis activity to identify developing tumors and angiogenesis related diseases. Furthermore, great need is also present for new molecular targets useful in the treatment of angiogenesis and angiogenesis related diseases such as cancer. In addition known modulators of angiogenesis such as endostatin or vascular endothelial growth factor (VEGF). Use of the methods and compositions disclosed herein in combination with anti-angiogenesis drugs, drugs that block the matrix breakdown (such as BMS-275291, Dalteparin (Fragmin®), Suramin), drugs that inhibit endothelial cells (2-methoxyestradiol (2-ME), CC-5013 (Thalidomide Analog), Combretastatin A4 Phosphate, LY317615 (Protein Kinase C Beta Inhibitor), Soy Isoflavone (Genistein; Soy Protein Isolate), Thalidomide), drugs that block activators of angiogenesis (AE-941 (Neovastat™; GW786034), Anti-VEGF Antibody (Bevacizumab; Avastin™), Interferon-alpha, PTK787/ZK 222584, VEGF-Trap, ZD6474), Drugs that inhibit endothelial-specific integrin/survival signaling (EMD 121974, Anti-Anb3 Integrin Antibody (Medi-522; Vitaxin™)).

Such a composition typically contains from about 0.1 to 90% by weight of a therapeutic agent of the invention formulated in and/or with a pharmaceutically acceptable carrier or excipient.

Pharmaceutical formulation is a well-established art that is further described in Gennaro (ed.), Remington: The Science and Practice of Pharmacy, 20th ed., Lippincott, Williams & Wilkins (2000); Ansel *et al.*, Pharmaceutical Dosage Forms and Drug Delivery Systems, 7th ed., Lippincott Williams & Wilkins (1999); and Kibbe (ed.), Handbook of Pharmaceutical Excipients American Pharmaceutical Association, 3rd ed. (2000) and thus need not be described in detail herein.

Briefly, formulation of the pharmaceutical compositions of the present invention will depend upon the route chosen for administration. The pharmaceutical compositions utilized in this invention can be administered by various routes including both enteral and parenteral routes, including oral, intravenous, intramuscular, subcutaneous, inhalation, topical, sublingual, rectal, intra-arterial, intramedullary, intrathecal, intraventricular, transmucosal, transdermal, intranasal, intraperitoneal, intrapulmonary, and intrauterine.

Oral dosage forms can be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions, and the like, for ingestion by the patient.

Solid formulations of the compositions for oral administration can contain suitable carriers or excipients, such as carbohydrate or protein fillers, such as sugars, including lactose, sucrose, mannitol, or sorbitol; starch from corn, wheat, rice, potato, or other plants; cellulose, such as methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, or microcrystalline cellulose; gums including arabic and tragacanth; proteins such as gelatin and collagen; inorganics, such as kaolin, calcium carbonate, dicalcium phosphate, sodium chloride; and other agents such as acacia and alginic acid.

Agents that facilitate disintegration and/or solubilization can be added, such as the cross-linked polyvinyl pyrrolidone, agar, alginic acid, or a salt thereof, such as sodium alginate, microcrystalline cellulose, cornstarch, sodium starch glycolate, and alginic acid.

Tablet binders that can be used include acacia, methylcellulose, sodium carboxymethylcellulose, polyvinylpyrrolidone (Povidone™), hydroxypropyl methylcellulose, sucrose, starch and ethylcellulose.

Lubricants that can be used include magnesium stearates, stearic acid, silicone fluid, talc, waxes, oils, and colloidal silica.

Fillers, agents that facilitate disintegration and/or solubilization, tablet binders and lubricants, including the aforementioned, can be used singly or in combination.

Solid oral dosage forms need not be uniform throughout. For example, dragee cores can be used in conjunction with suitable coatings, such as concentrated sugar solutions, which can also contain gum arabic, talc, polyvinylpyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures.

Oral dosage forms of the present invention include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a coating, such as glycerol or sorbitol. Push-fit capsules can contain active ingredients mixed with a filler or binders, such as lactose or starches, lubricants, such as talc or magnesium stearate, and, optionally, stabilizers. In soft capsules, the active compounds can be dissolved or suspended in suitable liquids, such as fatty oils, liquid, or liquid polyethylene glycol with or without stabilizers.

Additionally, dyestuffs or pigments can be added to the tablets or dragee coatings for product identification or to characterize the quantity of active compound, *i.e.*, dosage.

Liquid formulations of the pharmaceutical compositions for oral (enteral) administration are prepared in water or other aqueous vehicles and can contain various suspending agents such as methylcellulose, alginates, tragacanth, pectin, kelgin, carrageenan, acacia, polyvinylpyrrolidone, and polyvinyl alcohol. The liquid formulations can also include solutions, emulsions, syrups and elixirs containing, together with the active compound(s), wetting agents, sweeteners, and coloring and flavoring agents.

The pharmaceutical compositions of the present invention can also be formulated for parenteral administration. Formulations for parenteral administration can be in the form of aqueous or non-aqueous isotonic sterile injection solutions or suspensions.

For intravenous injection, water soluble versions of the compounds of the present invention are formulated in, or if provided as a lyophilate, mixed with, a physiologically acceptable fluid vehicle, such as 5% dextrose ("D5"), physiologically buffered saline, 0.9% saline, Hanks' solution, or Ringer's solution. Intravenous formulations may include carriers, excipients or stabilizers including, without limitation, calcium, human serum albumin, citrate, acetate, calcium chloride, carbonate, and other salts.

Intramuscular preparations, *e.g.* a sterile formulation of a suitable soluble salt form of the compounds of the present invention, can be dissolved and administered in a pharmaceutical excipient such as Water-for-Injection, 0.9% saline, or 5% glucose solution. Alternatively, a suitable insoluble form of the compound can be prepared and administered as a suspension in an aqueous base or a pharmaceutically acceptable oil base, such as an ester of a long chain fatty acid (*e.g.*, ethyl oleate), fatty oils such as sesame oil, triglycerides, or liposomes.

Parenteral formulations of the compositions can contain various carriers such as vegetable oils, dimethylacetamide, dimethylformamide, ethyl lactate, ethyl carbonate, isopropyl myristate, ethanol, polyols (glycerol, propylene glycol, liquid polyethylene glycol, and the like).

Aqueous injection suspensions can also contain substances that increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Non-lipid polycationic amino polymers can also be used for delivery. Optionally, the suspension can also contain suitable stabilizers or agents that increase the solubility of the compounds to allow for the preparation of highly concentrated solutions.

Pharmaceutical compositions of the present invention can also be formulated to permit injectable, long-term, deposition. Injectable depot forms may be made by forming microencapsulated matrices of the compound in biodegradable polymers such as polylactide-polyglycolide. Depending upon the ratio of drug to polymer and the nature of the particular polymer employed, the rate of drug release can be controlled. Examples of other biodegradable polymers include poly(orthoesters) and poly(anhydrides). Depot injectable formulations are also prepared by entrapping the drug in microemulsions that are compatible with body tissues.

The pharmaceutical compositions of the present invention can be administered topically. For topical use the compounds of the present invention can also be prepared in suitable forms to be applied to the skin, or mucus membranes of the nose and throat, and can take the form of lotions, creams, ointments, liquid sprays or inhalants, drops, tinctures, lozenges, or throat paints. Such topical formulations further can include chemical compounds such as dimethylsulfoxide (DMSO) to facilitate surface penetration of the active ingredient. In other transdermal formulations, typically in patch-delivered formulations, the pharmaceutically active compound is formulated with one or more skin penetrants, such as 2-N-methyl-pyrrolidone (NMP) or Azone. A topical semi-solid ointment formulation typically contains a concentration of the active ingredient from about 1 to 20%, *e.g.*, 5 to 10%, in a carrier such as a pharmaceutical cream base.

For application to the eyes or ears, the compounds of the present invention can be presented in liquid or semi-liquid form formulated in hydrophobic or hydrophilic bases as ointments, creams, lotions, paints or powders.

For rectal administration the compounds of the present invention can be administered in the form of suppositories admixed with conventional carriers such as cocoa butter, wax or other glyceride.

Inhalation formulations can also readily be formulated. For inhalation, various powder and liquid formulations can be prepared. For aerosol preparations, a sterile formulation of the compound or salt form of the compound may be used in inhalers, such as metered dose inhalers, and nebulizers. Aerosolized forms may be especially useful for treating respiratory disorders.

Alternatively, the compounds of the present invention can be in powder form for reconstitution in the appropriate pharmaceutically acceptable carrier at the time of delivery.

The pharmaceutically active compound in the pharmaceutical compositions of the present invention can be provided as the salt of a variety of acids, including but not limited to hydrochloric, sulfuric, acetic, lactic, tartaric, malic, and succinic acid. Salts tend to be more soluble in aqueous or other protonic solvents than are the corresponding free base forms.

After pharmaceutical compositions have been prepared, they are packaged in an appropriate container and labeled for treatment of an indicated condition.

The active compound will be present in an amount effective to achieve the intended purpose. The determination of an effective dose is well within the capability of those skilled in the art.

A "therapeutically effective dose" refers to that amount of active ingredient, for example OSP polypeptide, fusion protein, or fragments thereof, antibodies specific for OSP, agonists, antagonists or inhibitors of OSP, which ameliorates the signs or symptoms of the disease or prevent progression thereof; as would be understood in the medical arts, cure, although desired, is not required.

The therapeutically effective dose of the pharmaceutical agents of the present invention can be estimated initially by *in vitro* tests, such as cell culture assays, followed by assay in model animals, usually mice, rats, rabbits, dogs, or pigs. The animal model can also be used to determine an initial preferred concentration range and route of administration.

For example, the ED50 (the dose therapeutically effective in 50% of the population) and LD50 (the dose lethal to 50% of the population) can be determined in one or more cell culture of animal model systems. The dose ratio of toxic to therapeutic effects is the therapeutic index, which can be expressed as LD50/ED50. Pharmaceutical compositions that exhibit large therapeutic indices are preferred.

The data obtained from cell culture assays and animal studies are used in formulating an initial dosage range for human use, and preferably provide a range of circulating concentrations that includes the ED50 with little or no toxicity. After administration, or between successive administrations, the circulating concentration of active agent varies within this range depending upon pharmacokinetic factors well known in the art, such as the dosage form employed, sensitivity of the patient, and the route of administration.

The exact dosage will be determined by the practitioner, in light of factors specific to the subject requiring treatment. Factors that can be taken into account by the practitioner include the severity of the disease state, general health of the subject, age, weight, gender of the subject, diet, time and frequency of administration, drug combination(s), reaction sensitivities, and tolerance/response to therapy. Long-acting pharmaceutical compositions can be administered every 3 to 4 days, every week, or once every two weeks depending on half-life and clearance rate of the particular formulation.

Normal dosage amounts may vary from 0.1 to 100,000 micrograms, up to a total dose of about 1 g, depending upon the route of administration. Where the therapeutic agent is a protein or antibody of the present invention, the therapeutic protein or antibody agent typically is administered at a daily dosage of 0.01 mg to 30 mg/kg of body weight of the patient (*e.g.*, 1mg/kg to 5 mg/kg). The pharmaceutical formulation can be administered in multiple doses per day, if desired, to achieve the total desired daily dose.

Guidance as to particular dosages and methods of delivery is provided in the literature and generally available to practitioners in the art. Those skilled in the art will employ different formulations for nucleotides than for proteins or their inhibitors. Similarly, delivery of polynucleotides or polypeptides will be specific to particular cells, conditions, locations, etc.

Conventional methods, known to those of ordinary skill in the art of medicine, can be used to administer the pharmaceutical formulation(s) of the present invention to the patient. The pharmaceutical compositions of the present invention can be administered alone, or in combination with other therapeutic agents or interventions.

Therapeutic Methods

The present invention further provides methods of treating subjects having defects in a gene of the invention, *e.g.*, in expression, activity, distribution, localization, and/or solubility, which can manifest as a disorder of ovarian function. As used herein, “treating” includes all medically-acceptable types of therapeutic intervention, including palliation and prophylaxis (prevention) of disease. The term "treating" encompasses any improvement of a disease, including minor improvements. These methods are discussed below.

Gene Therapy and Vaccines

The isolated nucleic acids of the present invention can also be used to drive *in vivo* expression of the polypeptides of the present invention. *In vivo* expression can be driven from a vector, typically a viral vector, often a vector based upon a replication incompetent retrovirus, an adenovirus, or an adeno-associated virus (AAV), for the purpose of gene therapy. *In vivo* expression can also be driven from signals endogenous to the nucleic acid or from a vector, often a plasmid vector, such as pVAX1 (Invitrogen, Carlsbad, CA, USA), for purpose of "naked" nucleic acid vaccination, as further described in U.S. Patent Nos. 5,589,466; 5,679,647; 5,804,566; 5,830,877; 5,843,913; 5,880,104; 5,958,891; 5,985,847; 6,017,897; 6,110,898; 6,204,250, the disclosures of which are incorporated herein by reference in their entireties. For cancer therapy, it is preferred that the vector also be tumor-selective. *See, e.g.*, Doronin *et al.*, *J. Virol.* 75: 3314-24 (2001).

In another embodiment of the therapeutic methods of the present invention, a therapeutically effective amount of a pharmaceutical composition comprising a nucleic acid molecule of the present invention is administered. The nucleic acid molecule can be delivered in a vector that drives expression of an OSP, fusion protein, or fragment thereof, or without such vector. Nucleic acid compositions that can drive expression of an OSP are administered, for example, to complement a deficiency in the native OSP, or as DNA vaccines. Expression vectors derived from virus, replication deficient retroviruses, adenovirus, adeno-associated (AAV) virus, herpes virus, or vaccinia virus can be used as can plasmids. *See, e.g.*, Cid-Arregui, *supra*. In a preferred embodiment, the nucleic acid molecule encodes an OSP having the amino acid sequence of SEQ ID NO: 129-295, or a fragment, fusion protein, allelic variant or homolog thereof.

In still other therapeutic methods of the present invention, pharmaceutical compositions comprising host cells that express an OSP, fusions, or fragments thereof can be administered. In such cases, the cells are typically autologous, so as to circumvent xenogeneic or allotypic rejection, and are administered to complement defects in OSP production or activity. In a preferred embodiment, the nucleic acid molecules in the cells encode an OSP having the amino acid sequence of SEQ ID NO: 129-295, or a fragment, fusion protein, allelic variant or homolog thereof.

Antisense Administration

Antisense nucleic acid compositions, or vectors that drive expression of an OSG antisense nucleic acid, are administered to downregulate transcription and/or translation of an OSG in circumstances in which excessive production, or production of aberrant protein, is the pathophysiologic basis of disease.

Antisense compositions useful in therapy can have a sequence that is complementary to coding or to noncoding regions of an OSG. For example, oligonucleotides derived from the transcription initiation site, *e.g.*, between positions -10 and +10 from the start site, are preferred.

Catalytic antisense compositions, such as ribozymes, that are capable of sequence-specific hybridization to OSG transcripts, are also useful in therapy. *See, e.g.*, Phylactou, *Adv. Drug Deliv. Rev.* 44(2-3): 97-108 (2000); Phylactou *et al.*, *Hum. Mol. Genet.* 7(10): 1649-53 (1998); Rossi, *Ciba Found. Symp.* 209: 195-204 (1997); and Sigurdsson *et al.*, *Trends Biotechnol.* 13(8): 286-9 (1995).

Other nucleic acids useful in the therapeutic methods of the present invention are those that are capable of triplex helix formation in or near the OSG genomic locus. Such triplexing oligonucleotides are able to inhibit transcription. *See, e.g.*, Intody *et al.*, *Nucleic Acids Res.* 28(21): 4283-90 (2000); and McGuffie *et al.*, *Cancer Res.* 60(14): 3790-9 (2000). Pharmaceutical compositions comprising such triplex forming oligos (TFOs) are administered in circumstances in which excessive production, or production of aberrant protein, is a pathophysiologic basis of disease.

In a preferred embodiment, the antisense molecule is derived from a nucleic acid molecule encoding an OSP, preferably an OSP comprising an amino acid sequence of SEQ ID NO: 129-295, or a fragment, allelic variant or homolog thereof. In a more preferred embodiment, the antisense molecule is derived from a nucleic acid molecule having a nucleotide sequence of SEQ ID NO: 1-128, or a part, allelic variant, substantially similar or hybridizing nucleic acid thereof.

Polypeptide Administration

In one embodiment of the therapeutic methods of the present invention, a therapeutically effective amount of a pharmaceutical composition comprising an OSP, a fusion protein, fragment, analog or derivative thereof is administered to a subject with a clinically-significant OSP defect.

Protein compositions are administered, for example, to complement a deficiency in native OSP. In other embodiments, protein compositions are administered as a vaccine to elicit a humoral and/or cellular immune response to OSP. The immune response can be used to modulate activity of OSP or, depending on the immunogen, to immunize against aberrant or aberrantly expressed forms, such as mutant or inappropriately expressed isoforms. In yet other embodiments, protein fusions having a toxic moiety are administered to ablate cells that aberrantly accumulate OSP.

In a preferred embodiment, the polypeptide administered is an OSP comprising an amino acid sequence of SEQ ID NO: 129-295, or a fusion protein, allelic variant, homolog, analog or derivative thereof. In a more preferred embodiment, the polypeptide is encoded by a nucleic acid molecule having a nucleotide sequence of SEQ ID NO: 1-128, or a part, allelic variant, substantially similar or hybridizing nucleic acid thereof.

Antibody, Agonist and Antagonist Administration

In another embodiment of the therapeutic methods of the present invention, a therapeutically effective amount of a pharmaceutical composition comprising an antibody (including fragment or derivative thereof) of the present invention is administered. As is well known, antibody compositions are administered, for example, to antagonize activity of OSP, or to target therapeutic agents to sites of OSP presence and/or accumulation. In a preferred embodiment, the antibody specifically binds to an OSP comprising an amino acid sequence of SEQ ID NO: 129-295, or a fusion protein, allelic variant, homolog, analog or derivative thereof. In a more preferred embodiment, the antibody specifically binds to an OSP encoded by a nucleic acid molecule having a nucleotide sequence of SEQ ID NO: 1-128, or a part, allelic variant, substantially similar or hybridizing nucleic acid thereof.

The present invention also provides methods for identifying modulators which bind to an OSP or have a modulatory effect on the expression or activity of an OSP. Modulators which decrease the expression or activity of OSP (antagonists) are believed to be useful in treating ovarian cancer. Such screening assays are known to those of skill in the art and include, without limitation, cell-based assays and cell-free assays. Small molecules predicted via computer imaging to specifically bind to regions of an OSP can also be designed, synthesized and tested for use in the imaging and treatment of ovarian cancer. Further, libraries of molecules can be screened for potential anticancer agents by

assessing the ability of the molecule to bind to the OSPs identified herein. Molecules identified in the library as being capable of binding to an OSP are key candidates for further evaluation for use in the treatment of ovarian cancer. In a preferred embodiment, these molecules will downregulate expression and/or activity of an OSP in cells.

In another embodiment of the therapeutic methods of the present invention, a pharmaceutical composition comprising a non-antibody antagonist of OSP is administered. Antagonists of OSP can be produced using methods generally known in the art. In particular, purified OSP can be used to screen libraries of pharmaceutical agents, often combinatorial libraries of small molecules, to identify those that specifically bind and antagonize at least one activity of an OSP.

In other embodiments a pharmaceutical composition comprising an agonist of an OSP is administered. Agonists can be identified using methods analogous to those used to identify antagonists.

In a preferred embodiment, the antagonist or agonist specifically binds to and antagonizes or agonizes, respectively, an OSP comprising an amino acid sequence of SEQ ID NO: 129-295, or a fusion protein, allelic variant, homolog, analog or derivative thereof. In a more preferred embodiment, the antagonist or agonist specifically binds to and antagonizes or agonizes, respectively, an OSP encoded by a nucleic acid molecule having a nucleotide sequence of SEQ ID NO: 1-128, or a part, allelic variant, substantially similar or hybridizing nucleic acid thereof.

Targeting Ovarian Tissue

The invention also provides a method in which a polypeptide of the invention, or an antibody thereto, is linked to a therapeutic agent such that it can be delivered to the ovarian or to specific cells in the ovarian. In a preferred embodiment, an anti-OSP antibody is linked to a therapeutic agent and is administered to a patient in need of such therapeutic agent. The therapeutic agent may be a toxin, if ovarian tissue needs to be selectively destroyed. This would be useful for targeting and killing ovarian cancer cells. In another embodiment, the therapeutic agent may be a growth or differentiation factor, which would be useful for promoting ovarian cell function.

In another embodiment, an anti-OSP antibody may be linked to an imaging agent that can be detected using, *e.g.*, magnetic resonance imaging, CT or PET. This would be

useful for determining and monitoring ovarian function, identifying ovarian cancer tumors, and identifying noncancerous ovarian diseases.

EXAMPLES

Example 1a: Alternative Splice Variants

We identified gene transcripts using the Gencarta™ tools (Compugen Ltd., Tel Aviv, Israel) and a variety of public and proprietary databases. These splice variants are either sequences which differ from a previously defined sequence or new uses of known sequences. In general related variants are annotated as DEX0455_XXX.nt.1, DEX0455_XXX.nt.2, DEX0455_XXX.nt.3, etc. The variant DNA sequences encode proteins which differ from a previously defined protein sequence. In relation to the nucleotide sequence naming convention, protein variants are annotated as DEX0455_XXX.aa.1, DEX0455_XXX.aa.2, etc., wherein transcript DEX0455_XXX.nt.1 encodes protein DEX0455_XXX.aa.1. A single transcript may encode a protein from an alternate Open Reading Fram (ORF) which is designated DEX0455_XXX.orf.1. Additionally, multiple transcripts may encode for a single protein. In this case, DEX0455_XXX.nt.1 and DEX0455_XXX.nt.2 will both be associated with DEX0455_XXX.aa.1.

The mapping of the nucleic acid ("NT") SEQ ID NO; DEX ID; chromosomal location (if known); open reading frame (ORF) location; amino acid ("AA") SEQ ID NO; AA DEX ID; are shown in the table below.

SEQ ID NO	DEX ID	Chromo Map	ORF Loc	SEQ ID NO	DEX ID
1	DEX0455_001.nt.1	X;47722965-47733965	1624-2937	129	DEX0455_001.orf.1
1	DEX0455_001.nt.1	X;47722965-47733965	322-1035	130	DEX0455_001.aa.1
2	DEX0455_002.nt.1	17q11.1	217-915	131	DEX0455_002.aa.1
3	DEX0455_003.nt.1	10p11.23	132-476	132	DEX0455_003.aa.1
4	DEX0455_004.nt.1	3q29	7357-7809	133	DEX0455_004.orf.1
4	DEX0455_004.nt.1	3q29	2974-5074	134	DEX0455_004.aa.1
5	DEX0455_004.nt.2	3q29	6201-6653	135	DEX0455_004.orf.2
5	DEX0455_004.nt.2	3q29	2968-5257	136	DEX0455_004.aa.2
6	DEX0455_005.nt.1	2q13	854-1267	137	DEX0455_005.aa.1
7	DEX0455_005.nt.2	2q13	853-1270	137	DEX0455_005.aa.1
8	DEX0455_006.nt.1	9q22.1	730-1266	138	DEX0455_006.aa.1
9	DEX0455_007.nt.1	19q13.41	1-882	139	DEX0455_007.orf.1

9	DEX0455_007.nt.1	19q13.41	1-885	140	DEX0455_007.aa.1
10	DEX0455_008.nt.1	4q27	869-1138	141	DEX0455_008.aa.1
11	DEX0455_009.nt.1	20p12.2	1-1123	142	DEX0455_009.aa.1
12	DEX0455_010.nt.1	Un_6;1484154-1498876	341-784	143	DEX0455_010.orf.1
12	DEX0455_010.nt.1	Un_6;1484154-1498876	151-370	144	DEX0455_010.aa.1
13	DEX0455_010.nt.2	Un_6;1484154-1498876	49-621	145	DEX0455_010.orf.2
13	DEX0455_010.nt.2	Un_6;1484154-1498876	151-490	146	DEX0455_010.aa.2
14	DEX0455_011.nt.1	19q13.31	1-384	147	DEX0455_011.aa.1
15	DEX0455_012.nt.1	1q32.1	207-974	148	DEX0455_012.aa.1
16	DEX0455_012.nt.2	1q32.1	102-851	149	DEX0455_012.orf.2
16	DEX0455_012.nt.2	1q32.1	206-1415	150	DEX0455_012.aa.2
17	DEX0455_013.nt.1	12p12.3	10-666	151	DEX0455_013.aa.1
18	DEX0455_013.nt.2	12p12.3	124-639	152	DEX0455_013.aa.2
19	DEX0455_014.nt.1	1q42.2	880-1866	153	DEX0455_014.orf.1
19	DEX0455_014.nt.1	1q42.2	82-1870	154	DEX0455_014.aa.1
20	DEX0455_015.nt.1	12q13.2	1-255	155	DEX0455_015.aa.1
21	DEX0455_016.nt.1	1p31.1	104-868	156	DEX0455_016.aa.1
22	DEX0455_017.nt.1	1p33	102-623	157	DEX0455_017.aa.1
23	DEX0455_018.nt.1	9q34.11	209-1270	158	DEX0455_018.aa.1
24	DEX0455_018.nt.2	9q34.11	682-2148	159	DEX0455_018.aa.2
25	DEX0455_019.nt.1	11q13.4	66-926	160	DEX0455_019.aa.1
26	DEX0455_020.nt.1	19p13.11	365-793	161	DEX0455_020.aa.1
27	DEX0455_020.nt.2	19p13.11	688-1035	162	DEX0455_020.orf.2
27	DEX0455_020.nt.2	19p13.11	474-678	163	DEX0455_020.aa.2
28	DEX0455_021.nt.1	1p36.11	175-486	164	DEX0455_021.orf.1
28	DEX0455_021.nt.1	1p36.11	1-250	165	DEX0455_021.aa.1
29	DEX0455_021.nt.2	1p36.11	190-1269	166	DEX0455_021.aa.2
30	DEX0455_021.nt.3	1p36.11	46-1173	167	DEX0455_021.orf.3
30	DEX0455_021.nt.3	1p36.11	189-1590	168	DEX0455_021.aa.3
31	DEX0455_021.nt.4	1p36.11	190-1173	169	DEX0455_021.aa.4
32	DEX0455_022.nt.1	19p13.12	109-642	170	DEX0455_022.aa.1
33	DEX0455_022.nt.2	19p13.12	70-492	171	DEX0455_022.orf.2
33	DEX0455_022.nt.2	19p13.12	108-675	172	DEX0455_022.aa.2
34	DEX0455_022.nt.3	19p13.12	91-324	173	DEX0455_022.aa.3
35	DEX0455_023.nt.1	7q11.21	609-956	174	DEX0455_023.aa.1
36	DEX0455_024.nt.1	2p13.3	486-1569	175	DEX0455_024.aa.1
37	DEX0455_024.nt.2	2p13.3	469-999	176	DEX0455_024.aa.2
38	DEX0455_025.nt.1	17q24.3	475-1614	177	DEX0455_025.aa.1
39	DEX0455_025.nt.2	17q24.3	328-1509	178	DEX0455_025.orf.2
39	DEX0455_025.nt.2	17q24.3	474-2514	179	DEX0455_025.aa.2
40	DEX0455_025.nt.3	17q24.3	474-1617	177	DEX0455_025.aa.1
41	DEX0455_025.nt.4	17q24.3	474-1617	177	DEX0455_025.aa.1
42	DEX0455_026.nt.1	2q32.2	3-218	180	DEX0455_026.orf.1
42	DEX0455_026.nt.1	2q32.2	1-236	181	DEX0455_026.aa.1

43	DEX0455_027.nt.1	2q24.3	986-1507	182	DEX0455_027.orf.1
43	DEX0455_027.nt.1	2q24.3	16-128	183	DEX0455_027.aa.1
44	DEX0455_028.nt.1	9p24.3	141-785	184	DEX0455_028.aa.1
45	DEX0455_029.nt.1	9q21.11	4134-4532	185	DEX0455_029.orf.1
45	DEX0455_029.nt.1	9q21.11	2985-5847	186	DEX0455_029.aa.1
46	DEX0455_029.nt.2	9q21.11	4562-5143	187	DEX0455_029.orf.2
46	DEX0455_029.nt.2	9q21.11	2962-5149	188	DEX0455_029.aa.2
47	DEX0455_030.nt.1	16p11.2	188-1123	189	DEX0455_030.aa.1
48	DEX0455_030.nt.2	16p11.2	82-627	190	DEX0455_030.aa.2
49	DEX0455_031.nt.1	12p13.31	135-1013	191	DEX0455_031.orf.1
49	DEX0455_031.nt.1	12p13.31	248-2156	192	DEX0455_031.aa.1
50	DEX0455_031.nt.2	12p13.31	248-749	193	DEX0455_031.aa.2
50	DEX0455_031.nt.2	12p13.31	1325-2239	194	DEX0455_031.orf.2
51	DEX0455_031.nt.3	12p13.31	1-582	195	DEX0455_031.aa.3
52	DEX0455_032.nt.1	7q31.1	39-761	196	DEX0455_032.aa.1
53	DEX0455_033.nt.1	1p34.1	161-943	197	DEX0455_033.aa.1
54	DEX0455_034.nt.1	15q21.1	197-1693	198	DEX0455_034.aa.1
55	DEX0455_034.nt.2	15q21.1	1-1497	198	DEX0455_034.aa.1
56	DEX0455_034.nt.3	15q21.1	197-1228	199	DEX0455_034.aa.3
57	DEX0455_034.nt.4	15q21.1	2-1438	200	DEX0455_034.aa.4
58	DEX0455_035.nt.1	10q22.1	102-464	201	DEX0455_035.aa.1
59	DEX0455_035.nt.2	10q22.1	755-1201	202	DEX0455_035.orf.2
59	DEX0455_035.nt.2	10q22.1	330-696	203	DEX0455_035.aa.2
60	DEX0455_035.nt.3	10q22.1	634-1080	204	DEX0455_035.orf.3
60	DEX0455_035.nt.3	10q22.1	269-575	205	DEX0455_035.aa.3
61	DEX0455_036.nt.1	19p13.2	86-370	206	DEX0455_036.orf.1
61	DEX0455_036.nt.1	19p13.2	58-389	207	DEX0455_036.aa.1
62	DEX0455_036.nt.2	19p13.2	295-4749	208	DEX0455_036.aa.2
63	DEX0455_036.nt.3	19p13.2	3-335	209	DEX0455_036.orf.3
63	DEX0455_036.nt.3	19p13.2	88-352	210	DEX0455_036.aa.3
64	DEX0455_036.nt.4	19p13.2	77-352	211	DEX0455_036.orf.4
64	DEX0455_036.nt.4	19p13.2	1-253	212	DEX0455_036.aa.4
65	DEX0455_037.nt.1	9	113-787	213	DEX0455_037.aa.1
66	DEX0455_037.nt.2	9	2-1048	214	DEX0455_037.orf.2
66	DEX0455_037.nt.2	9	112-1354	215	DEX0455_037.aa.2
67	DEX0455_037.nt.3	9	113-1342	216	DEX0455_037.aa.3
68	DEX0455_037.nt.4	9	2-410	217	DEX0455_037.aa.4
69	DEX0455_037.nt.5	9	3-452	218	DEX0455_037.aa.5
70	DEX0455_037.nt.6	9	113-784	219	DEX0455_037.aa.6
71	DEX0455_037.nt.7	9	113-1555	220	DEX0455_037.aa.7
72	DEX0455_038.nt.1	20p12.1	298-3561	221	DEX0455_038.aa.1
73	DEX0455_038.nt.2	20p12.1	298-3564	221	DEX0455_038.aa.1
74	DEX0455_038.nt.3	20p12.1	1-1320	222	DEX0455_038.orf.3
74	DEX0455_038.nt.3	20p12.1	298-1863	223	DEX0455_038.aa.3
75	DEX0455_039.nt.1	19q13.2	2-496	224	DEX0455_039.aa.1
76	DEX0455_039.nt.2	19q13.2	2-787	225	DEX0455_039.aa.2
77	DEX0455_040.nt.1	19q13.2	299-991	226	DEX0455_040.orf.1

77	DEX0455_040.nt.1	19q13.2	352-991	227	DEX0455_040.aa.1
78	DEX0455_040.nt.2	19q13.2	770-1495	228	DEX0455_040.aa.2
79	DEX0455_041.nt.1	20q11.23	54-212	229	DEX0455_041.orf.1
79	DEX0455_041.nt.1	20q11.23	7-138	230	DEX0455_041.aa.1
80	DEX0455_041.nt.2	20q11.23	11-208	231	DEX0455_041.orf.2
80	DEX0455_041.nt.2	20q11.23	1-107	232	DEX0455_041.aa.2
81	DEX0455_042.nt.1	4q22.1	90-437	233	DEX0455_042.orf.1
81	DEX0455_042.nt.1	4q22.1	70-439	234	DEX0455_042.aa.1
82	DEX0455_043.nt.1	1q42.12	511-768	235	DEX0455_043.orf.1
82	DEX0455_043.nt.1	1q42.12	1-93	236	DEX0455_043.aa.1
83	DEX0455_043.nt.2	1q42.12	413-787	237	DEX0455_043.orf.2
83	DEX0455_043.nt.2	1q42.12	1-93	236	DEX0455_043.aa.1
84	DEX0455_043.nt.3	1q42.12	1220-1531	238	DEX0455_043.orf.3
84	DEX0455_043.nt.3	1q42.12	1-93	236	DEX0455_043.aa.1
85	DEX0455_044.nt.1	17q25.3	445-627	239	DEX0455_044.aa.1
86	DEX0455_045.nt.1	16p12.3	1-579	240	DEX0455_045.orf.1
86	DEX0455_045.nt.1	16p12.3	1-492	241	DEX0455_045.aa.1
87	DEX0455_046.nt.1	17q21.32	709-1389	242	DEX0455_046.orf.1
87	DEX0455_046.nt.1	17q21.32	802-1389	243	DEX0455_046.aa.1
88	DEX0455_047.nt.1	8p23.1	2887-3195	244	DEX0455_047.orf.1
88	DEX0455_047.nt.1	8p23.1	136-334	245	DEX0455_047.aa.1
89	DEX0455_047.nt.2	8p23.1	1091-1399	246	DEX0455_047.orf.2
89	DEX0455_047.nt.2	8p23.1	19-102	247	DEX0455_047.aa.2
90	DEX0455_048.nt.1	X;150645762-150649651	84-545	248	DEX0455_048.aa.1
91	DEX0455_048.nt.2	X;150645762-150649651	286-813	249	DEX0455_048.orf.2
91	DEX0455_048.nt.2	X;150645762-150649651	1-817	250	DEX0455_048.aa.2
92	DEX0455_049.nt.1	2p21	1183-1986	251	DEX0455_049.aa.1
93	DEX0455_049.nt.2	2p21	378-1403	252	DEX0455_049.aa.2
94	DEX0455_049.nt.3	2p21	808-1527	253	DEX0455_049.aa.3
95	DEX0455_049.nt.4	2p21	1-1170	254	DEX0455_049.aa.4
96	DEX0455_049.nt.5	2p21	179-1120	255	DEX0455_049.aa.5
97	DEX0455_050.nt.1	7p22.1	186-551	256	DEX0455_050.orf.1
97	DEX0455_050.nt.1	7p22.1	1-149	257	DEX0455_050.aa.1
98	DEX0455_051.nt.1	19	1-1788	258	DEX0455_051.aa.1
99	DEX0455_051.nt.2	19	1-1224	259	DEX0455_051.aa.2
100	DEX0455_051.nt.3	19	1-1410	260	DEX0455_051.aa.3
101	DEX0455_051.nt.4	19	1-1224	259	DEX0455_051.aa.2
101	DEX0455_051.nt.4	19	1-1422	261	DEX0455_051.orf.4
102	DEX0455_051.nt.5	19	1-1224	259	DEX0455_051.aa.2
102	DEX0455_051.nt.5	19	1-1422	262	DEX0455_051.orf.5
103	DEX0455_051.nt.6	19	1-1224	259	DEX0455_051.aa.2
103	DEX0455_051.nt.6	19	1-1422	263	DEX0455_051.orf.6
104	DEX0455_052.nt.1	19	13-1422	264	DEX0455_052.aa.1
105	DEX0455_052.nt.2	19	13-1518	265	DEX0455_052.aa.2
106	DEX0455_052.nt.3	19	188-1831	266	DEX0455_052.aa.3

107	DEX0455_052.nt.4	19	100-930	267	DEX0455_052.aa.4
108	DEX0455_053.nt.1	1p12	1-846	268	DEX0455_053.aa.1
109	DEX0455_053.nt.2	1p12	1-177	269	DEX0455_053.aa.2
109	DEX0455_053.nt.2	1p12	253-1008	270	DEX0455_053.aa.3
110	DEX0455_054.nt.1	15q24.3	1218-1682	271	DEX0455_054.orf.1
110	DEX0455_054.nt.1	15q24.3	1038-1362	272	DEX0455_054.aa.1
111	DEX0455_054.nt.2	15q24.3	410-874	273	DEX0455_054.orf.2
111	DEX0455_054.nt.2	15q24.3	122-554	274	DEX0455_054.aa.2
112	DEX0455_055.nt.1	1	812-1570	275	DEX0455_055.aa.1
113	DEX0455_055.nt.2	1	388-1470	276	DEX0455_055.aa.2
114	DEX0455_055.nt.3	1p34.2	402-902	277	DEX0455_055.aa.3
115	DEX0455_056.nt.1	7q31.1	626-2533	278	DEX0455_056.orf.1
115	DEX0455_056.nt.1	7q31.1	670-3283	279	DEX0455_056.aa.1
116	DEX0455_056.nt.2	7q31.1	671-3043	280	DEX0455_056.aa.2
117	DEX0455_057.nt.1	1q21.3	146-511	281	DEX0455_057.orf.1
117	DEX0455_057.nt.1	1q21.3	1-513	282	DEX0455_057.aa.1
118	DEX0455_057.nt.2	1q21.3	405-681	283	DEX0455_057.aa.2
119	DEX0455_058.nt.1	1q42.12	1208-1405	284	DEX0455_058.orf.1
119	DEX0455_058.nt.1	1q42.12	315-513	285	DEX0455_058.aa.1
120	DEX0455_059.nt.1	19p13.11	294-1382	286	DEX0455_059.orf.1
120	DEX0455_059.nt.1	19p13.11	1-352	287	DEX0455_059.aa.1
121	DEX0455_059.nt.2	19p13.11	596-1093	288	DEX0455_059.orf.2
121	DEX0455_059.nt.2	19p13.11	1-352	287	DEX0455_059.aa.1
122	DEX0455_060.nt.1	21q21.1	3-623	289	DEX0455_060.aa.1
123	DEX0455_061.nt.1	10q11.21	1564-2619	290	DEX0455_061.aa.1
124	DEX0455_061.nt.2	10q11.21	2449-3231	291	DEX0455_061.aa.2
125	DEX0455_061.nt.3	10q11.21	2449-3255	292	DEX0455_061.aa.3
126	DEX0455_061.nt.4	10q11.21	1045-1443	293	DEX0455_061.aa.4
127	DEX0455_061.nt.5	10q11.21	842-1330	294	DEX0455_061.orf.5
127	DEX0455_061.nt.5	10q11.21	1740-2142	293	DEX0455_061.aa.4
128	DEX0455_062.nt.1	2p25.1	120-1592	295	DEX0455_062.aa.1

The polypeptides of the present invention were analyzed and the following attributes were identified; specifically, epitopes, post translational modifications, signal peptides and transmembrane domains. Antigenicity (Epitope) prediction was performed through the antigenic module in the EMBOSS package. Rice, P., EMBOSS: The European Molecular Biology Open Software Suite, *Trends in Genetics* 16(6): 276-277 (2000). The antigenic module predicts potentially antigenic regions of a protein sequence, using the method of Kolaskar and Tongaonkar. Kolaskar, AS and Tongaonkar, PC., A semi-empirical method for prediction of antigenic determinants on protein antigens, *FEBS Letters* 276: 172-174 (1990). Examples of post-translational modifications (PTMs) and other motifs of the OSPs of this invention are listed below. In addition, antibodies that specifically bind such post-translational modifications may be useful as a diagnostic or as

therapeutic. The PTMs and other motifs were predicted by using the ProSite Dictionary of Proteins Sites and Patterns (Bairoch *et al.*, *Nucleic Acids Res.* 25(1):217-221 (1997)), the following motifs, including PTMs, were predicted for the OSPs of the invention. The signal peptides were detected by using the SignalP 2.0, *see* Nielsen *et al.*, *Protein Engineering* 12, 3-9 (1999). Prediction of transmembrane helices in proteins was performed by the application TMHMM 2.0, "currently the best performing transmembrane prediction program", according to authors (Krogh *et al.*, *Journal of Molecular Biology*, 305(3):567-580, (2001); Moller *et al.*, *Bioinformatics*, 17(7):646-653, (2001); Sonnhammer, *et al.*, *A hidden Markov model for predicting transmembrane helices in protein sequences* in Glasgow, *et al.* Ed. Proceedings of the Sixth International Conference on Intelligent Systems for Molecular Biology, pages 175-182, Menlo Park, CA, 1998. AAAI Press. The PSORT II program may also be used to predict cellular localizations. Horton et al., *Intelligent Systems for Molecular Biology* 5: 147-152 (1997). The table below includes the following sequence annotations: Signal peptide presence; TM (number of membrane domain, topology in orientation and position); Amino acid location and antigenic index (location, AI score); PTM and other motifs (type, amino acid residue locations); and functional domains (type, amino acid residue locations).

DEX ID	Sig P	TMHMM	Antigenicity	PTM	Domains
DEX0455_001.orf.1	N	o - o1-438;	333-345,1.127; 155-162,1.105; 184-208,1.14; 231-239,1.049; 56-63,1.067; 170-176,1.117; 38-47,1.115; 75-81,1.069; 108-119,1.16; 305-311,1.041; 273-283,1.106; 241-256,1.161; 4-36.1.186:	CK2_PHOSPHO_SITE 104-107; PKC_PHOSPHO_SITE 284-286; CAMP_PHOSPHO_SITE 85-88; CK2_PHOSPHO_SITE 352-355; CK2_PHOSPHO_SITE 43-46; PKC_PHOSPHO_SITE 430-432; MYRISTYL 138-143; MYRISTYL 265-270; ASN_GLYCOSYLATION 167-170; PKC_PHOSPHO_SITE 216-218; MYRISTYL 260-265; TYR_PHOSPHO_SITE 200-206; MYRISTYL 179-184; PKC_PHOSPHO_SITE 84-86; PKC_PHOSPHO_SITE 153-155; PKC_PHOSPHO_SITE 163-165; CK2_PHOSPHO_SITE 284-287; MYRISTYL 267-272;	PRICHEXTENSN 111-128; PRO_RICH_2 185-351; PRICHEXTENSN 1-13; PRICHEXTENSN 63-75; PRICHEXTENSN 206-231; PRO_RICH_1 1-75;

			323-329,1.094; 290-302,1.123; 383-435,1.147; 122-131,1.09; 211-217,1.039;		
DEX0455_001.aa.1	N	0 - o1-237;	164-217,1.189; 14-30,1.076; 79-85,1.054; 64-74,1.136; 148-161,1.094; 89-114,1.145; 116-138,1.139; 43-61,1.159; 33-39,1.034; 4-11,1.088;	MYRISTYL 194-199; MYRISTYL 5-10; PKC_PHOSPHO_SITE 88-90; PKC_PHOSPHO_SITE 47-49; CK2_PHOSPHO_SITE 41-44; LEUCINE_ZIPPER 157-178; MYRISTYL 198-203; PKC_PHOSPHO_SITE 29-31; MYRISTYL 187-192; PKC_PHOSPHO_SITE 235-237; CK2_PHOSPHO_SITE 205-208;	
DEX0455_002.aa.1	N	0 - o1-233;	174-212,1.218; 88-148,1.133; 153-158,1.07; 67-81,1.137; 46-65,1.141; 9-44,1.202;	CK2_PHOSPHO_SITE 159-162; MYRISTYL 139-144; MYRISTYL 112-117; MYRISTYL 83-88; ASN_GLYCOSYLATION 47-50; MYRISTYL 181-186; MYRISTYL 61-66;	TONB_DEPENDENT_REC_1 1-49; GALAPTIN 165-186; GLECT 103-233; Gal-bind_lectin 104-233;
DEX0455_003.aa.1	N	0 - o1-115;	9-18,1.083; 30-51,1.14; 56-82,1.155; 104-111,1.084;	CAMP_PHOSPHO_SITE 21-24; CK2_PHOSPHO_SITE 24-27; MYRISTYL 57-62; PKC_PHOSPHO_SITE 32-34; CK2_PHOSPHO_SITE 43-46; MYRISTYL 25-30; PKC_PHOSPHO_SITE 4-6; AMIDATION 101-104; PKC_PHOSPHO_SITE 93-95; PKC_PHOSPHO_SITE 109-111; AMIDATION 4-7;	ARG_RICH 18-104;
DEX0455_004.orf.1	N	1 - o1-54;tm55-74;i75	112-143,1.199; 5-12,1.074; 40-	MYRISTYL 96-101; PKC_PHOSPHO_SITE 145-147; MYRISTYL 82-87; MYRISTYL 105-110; PKC_PHOSPHO_SITE 25-27; CK2_PHOSPHO_SITE	

		-151;	104,1.27; 14-37,1.097;	143-146;	
DEX0455_004.aa.1	N	2 - o1-594;tm595-617;i618-666;tm667-689;o690-699;	245-261,1.17; 51-68,1.161; 429-437,1.15; 202-222,1.139; 533-553,1.095; 102-115,1.182; 186-193,1.076; 121-140,1.245; 333-341,1.129; 375-383,1.117; 265-319,1.148; 142-174,1.138; 70-98,1.151; 345-354,1.089; 579-588,1.236; 445-458,1.242; 515-531,1.129; 398-405,1.098; 690-696,1.182; 593-617,1.232; 224-243,1.183; 629-688,1.194; 408-413,1.058; 475-512,1.147; 462-473,1.227; 23-34,1.175; 363-369,1.038;	CK2_PHOSPHO_SITE 440-443; CK2_PHOSPHO_SITE 36-39; PKC_PHOSPHO_SITE 641-643; MYRISTYL 264-269; PKC_PHOSPHO_SITE 28-30; ASN_GLYCOSYLATION 471-474; ASN_GLYCOSYLATION 628-631; MYRISTYL 591-596; PKC_PHOSPHO_SITE 210-212; CAMP_PHOSPHO_SITE 15-18; ASN_GLYCOSYLATION 569-572; CK2_PHOSPHO_SITE 140-143; PKC_PHOSPHO_SITE 302-304; MYRISTYL 557-562; AMIDATION 19-22; ASN_GLYCOSYLATION 297-300; AMIDATION 197-200; CAMP_PHOSPHO_SITE 587-590; CK2_PHOSPHO_SITE 542-545; PKC_PHOSPHO_SITE 420-422; PKC_PHOSPHO_SITE 70-72; MYRISTYL 530-535; PKC_PHOSPHO_SITE 560-562; MYRISTYL 256-261; CAMP_PHOSPHO_SITE 16-19; MYRISTYL 625-630; PKC_PHOSPHO_SITE 527-529; MYRISTYL 93-98; PKC_PHOSPHO_SITE 19-21; PKC_PHOSPHO_SITE 514-516; TYR_PHOSPHO_SITE 149-155;	RIBOSOMAL_S2_1 245-256; LYS_RICH 9-22;
DEX0455_004.or	N	1 - o1-	14-37.1.097:	CK2_PHOSPHO_SITE 143-146; MYRISTYL 96-101:	

f.2		54;tm55-74;i75-151;	40-104,1.27;112-143,1.199;5-12,1.074;	PKC_PHOSPHO_SITE 25-27; MYRISTYL 105-110; MYRISTYL 82-87; PKC_PHOSPHO_SITE 145-147;	
DEX0455_004.aa.2	N	9 -o1-210;tm211-233;i234-282;tm283-305;o306-324;tm325-347;i348-367;tm368-385;o386-543;tm544-566;i567-578;tm579-599;o600-613;tm614-633;i634-679;tm680-699;o700-703;tm704-721;i722-762;	713-724,1.168;19-28,1.088;131-153,1.129;746-755,1.027;209-233,1.232;604-653,1.189;78-89,1.227;484-491,1.123;402-459,1.205;497-519,1.232;367-394,1.253;195-204,1.236;91-128,1.147;657-705,1.254;245-313,1.194;577-601,1.285;555-569,1.252;523-553,1.135;737-744,1.1;61-74,1.242;156-169,1.143;45-53,1.15;323-353,1.237;472-480,1.153;	PKC_PHOSPHO_SITE 257-259; MYRISTYL 14-19; MYRISTYL 173-178; CK2_PHOSPHO_SITE 676-679; PKC_PHOSPHO_SITE 620-622; PKC_PHOSPHO_SITE 143-145; ASN_GLYCOSYLATION 418-421; PKC_PHOSPHO_SITE 176-178; MYRISTYL 207-212; ASN_GLYCOSYLATION 87-90; CAMP_PHOSPHO_SITE 203-206; MYRISTYL 161-166; MYRISTYL 13-18; ASN_GLYCOSYLATION 493-496; MYRISTYL 691-696; TYR_PHOSPHO_SITE 755-761; PKC_PHOSPHO_SITE 676-678; MYRISTYL 241-246; ASN_GLYCOSYLATION 363-366; CK2_PHOSPHO_SITE 466-469; PKC_PHOSPHO_SITE 594-596; ASN_GLYCOSYLATION 312-315; ASN_GLYCOSYLATION 244-247; CK2_PHOSPHO_SITE 56-59; CK2_PHOSPHO_SITE 320-323; CK2_PHOSPHO_SITE 506-509; PKC_PHOSPHO_SITE 425-427; PKC_PHOSPHO_SITE 721-723; MYRISTYL 712-717; PKC_PHOSPHO_SITE 130-132; ASN_GLYCOSYLATION 185-188; PKC_PHOSPHO_SITE 506-508;	N4_MTASE 609-614;
DEX0455_005.aa.1	N	0 -o1-138;	19-29,1.121;125-132,1.063;4-9,1.045;	PKC_PHOSPHO_SITE 87-89; MYRISTYL 21-26; PKC_PHOSPHO_SITE 131-133; MYRISTYL 102-107; CK2_PHOSPHO_SITE 38-41;	

			45-61,1.116; 88-107,1.22; 76-85,1.064;	CK2_PHOSPHO_SITE 29-32;	
DEX0455_006.aa.1	N	0 - o1-179;	34-45,1.149; 92-99,1.162; 8-14,1.034; 117-135,1.172; 49-61,1.175; 168-176,1.097; 104-110,1.069; 77-85,1.119; 143-155,1.15;	CAMP_PHOSPHO_SITE 62-65; CK2_PHOSPHO_SITE 110-113; AMIDATION 138-141; CK2_PHOSPHO_SITE 67-70; TYR_PHOSPHO_SITE 88-95; CK2_PHOSPHO_SITE 74-77; PKC_PHOSPHO_SITE 112-114; MYRISTYL 36-41; CAMP_PHOSPHO_SITE 127-130; CK2_PHOSPHO_SITE 106-109; MYRISTYL 133-138;	
DEX0455_007.orf.1	N	0 - o1-294;	4-23,1.139; 194-201,1.095; 133-176,1.151; 39-45,1.069; 58-68,1.056; 244-261,1.123; 78-120,1.147;	PKC_PHOSPHO_SITE 24-26; CK2_PHOSPHO_SITE 71-74; MYRISTYL 231-236; CK2_PHOSPHO_SITE 203-206; PKC_PHOSPHO_SITE 270-272; PKC_PHOSPHO_SITE 131-133; CK2_PHOSPHO_SITE 189-192; MYRISTYL 278-283; CK2_PHOSPHO_SITE 24-27; MYRISTYL 201-206; MYRISTYL 266-271; MYRISTYL 120-125; CK2_PHOSPHO_SITE 56-59; CAMP_PHOSPHO_SITE 132-135;	
DEX0455_007.aa.1	N	0 - o1-294;	4-23,1.139; 133-176,1.151; 194-201,1.095; 39-45,1.069; 244-261,1.123; 58-68,1.056; 78-120,1.147;	MYRISTYL 266-271; CAMP_PHOSPHO_SITE 132-135; PKC_PHOSPHO_SITE 131-133; MYRISTYL 278-283; CK2_PHOSPHO_SITE 24-27; MYRISTYL 120-125; CK2_PHOSPHO_SITE 189-192; MYRISTYL 201-206; CK2_PHOSPHO_SITE 71-74; PKC_PHOSPHO_SITE 270-272; CK2_PHOSPHO_SITE 203-206; MYRISTYL 231-236; PKC_PHOSPHO_SITE 24-26; CK2_PHOSPHO_SITE 56-59;	
DEX0455_008.aa.1	N	0 - o1-90;	43-78,1.171; 16-37,1.092;	CK2_PHOSPHO_SITE 57-60; PKC_PHOSPHO_SITE 79-81; MYRISTYL 36-41; CAMP_PHOSPHO_SITE 81-84; PKC_PHOSPHO_SITE 12-14;	HORMA 14-72;
DEX0455	N	1 -	189-	MYRISTYL 335-340; MYRISTYL	LAMP 1 149-163;

_009.aa.1		o1-328;tm329-351;i352-373;	217,1.126;139-145,1.097;258-270,1.167;38-61,1.154;272-286,1.083;156-177,1.157;73-122,1.145;231-240,1.152;289-321,1.16;328-354,1.187;4-32,1.238;247-253,1.064;	83-88; PKC_PHOSPHO_SITE 241-243; ASN_GLYCOSYLATION 146-149; MYRISTYL 34-39; MYRISTYL 32-37; PKC_PHOSPHO_SITE 228-230; AMIDATION 51-54; PKC_PHOSPHO_SITE 4-6; CK2_PHOSPHO_SITE 195-198; ASN_GLYCOSYLATION 220-223; PKC_PHOSPHO_SITE 13-15; CK2_PHOSPHO_SITE 134-137;	LYSASSOCTDMP 139-163; LYSASSOCTDMP 267-281;
DEX0455_010.orf.1	N	1 - o1-109;tm110-132;i133-148;	51-57,1.138;78-98,1.159;111-132,1.193;4-41,1.243;67-75,1.122;	MYRISTYL 57-62; MYRISTYL 52-57; MYRISTYL 140-145;	IG_LIKE 8-112; IGc1 23-94; ig 21-86; IG_MHC 82-88;
DEX0455_010.aa.1	N	0 - o1-72;	4-12,1.148;34-44,1.09;55-69,1.084;22-28,1.112;	TYR_PHOSPHO_SITE 50-58; CK2_PHOSPHO_SITE 37-40; PKC_PHOSPHO_SITE 37-39;	sp_P13761_HB2J_HUMAN 43-70;
DEX0455_010.orf.2	Y	2 - o1-14;tm15-37;i38-152;tm153-175;o176-191;	94-100,1.138;4-84,1.243;154-175,1.193;121-141,1.159;110-118,1.122;	MYRISTYL 24-29; MYRISTYL 95-100; MYRISTYL 100-105; MYRISTYL 183-188;	IGc1 66-137; ig 64-129; IG_MHC 125-131; IG_LIKE 51-155;
DEX0455_010.aa.2	N	0 - o1-112;	87-103,1.09;60-66,1.138;4-50.1.243:	MYRISTYL 107-112; MYRISTYL 61-66; MYRISTYL 66-71; CK2_PHOSPHO_SITE 106-109; MYRISTYL 96-101;	IG_LIKE 17-112; IGc1 32-103; ig 30-95;

			76-84,1.122;		
DEX0455_011.aa.1	N	0 - o1-128;	78-97,1.118; 99-115,1.098; 7-33,1.125; 37-43,1.08; 118-125,1.159;	PKC_PHOSPHO_SITE 82-84; ASN_GLYCOSYLATION 48-51; CAMP_PHOSPHO_SITE 66-69; MYRISTYL 59-64; ASN_GLYCOSYLATION 58-61; CK2_PHOSPHO_SITE 34-37;	GALAPTIN 61-81; SUI1_1 115-122; GLECT 4-128; Gal-bind_lectin 1-128;
DEX0455_012.aa.1	N	0 - o1-256;	136-143,1.08; 193-199,1.037; 176-189,1.099; 69-82,1.102; 38-45,1.131; 87-93,1.067; 4-9,1.066; 100-128,1.153; 26-34,1.129; 236-245,1.062;	CK2_PHOSPHO_SITE 20-23; CK2_PHOSPHO_SITE 215-218; MYRISTYL 202-207; CK2_PHOSPHO_SITE 132-135; CK2_PHOSPHO_SITE 131-134; MYRISTYL 200-205; CK2_PHOSPHO_SITE 93-96; MYRISTYL 53-58; CK2_PHOSPHO_SITE 88-91; MYRISTYL 182-187; CAMP_PHOSPHO_SITE 237-240; MYRISTYL 162-167; MYRISTYL 249-254; PKC_PHOSPHO_SITE 54-56; MYRISTYL 99-104;	SAM_PNT 48-132; SAM_PNT 48-132;
DEX0455_012.orf.2	N	0 - o1-250;	4-10,1.07; 104-117,1.102; 240-246,1.107; 135-163,1.153; 16-32,1.09; 61-69,1.129; 228-234,1.037; 73-80,1.131; 122-128,1.067; 171-178,1.08; 37-44,1.077; 211-224,1.099;	CK2_PHOSPHO_SITE 166-169; MYRISTYL 1-6; MYRISTYL 134-139; MYRISTYL 217-222; MYRISTYL 197-202; CK2_PHOSPHO_SITE 167-170; MYRISTYL 88-93; CK2_PHOSPHO_SITE 238-241; PKC_PHOSPHO_SITE 89-91; CK2_PHOSPHO_SITE 128-131; PKC_PHOSPHO_SITE 11-13; MYRISTYL 28-33; MYRISTYL 22-27; CK2_PHOSPHO_SITE 123-126; MYRISTYL 33-38; MYRISTYL 235-240; CK2_PHOSPHO_SITE 55-58;	SAM_PNT 83-167; SAM_PNT 83-167;
DEX0455_012.aa.2	N	0 - o1-402;	176-189,1.099; 38-45,1.131;	AMIDATION 273-276; MYRISTYL 53-58; AMIDATION 377-380; CK2_PHOSPHO_SITE 246-249; MYRISTYL 99-104;	ETSDOMAIN 330-348; ETSDOMAIN 349-367; ETSDOMAIN 304-

			288-294,1.052; 26-34,1.129; 69-82,1.102; 205-218,1.129; 100-128,1.153; 136-143,1.08; 311-318,1.118; 4-9,1.066; 87-93,1.067; 379-385,1.088; 193-199,1.037; 332-346,1.091;	CK2_PHOSPHO_SITE 224-227; MYRISTYL 162-167; CK2_PHOSPHO_SITE 203-206; PKC_PHOSPHO_SITE 54-56; ASN_GLYCOSYLATION 388-391; CK2_PHOSPHO_SITE 213-216; CK2_PHOSPHO_SITE 88-91; MYRISTYL 182-187; ASN_GLYCOSYLATION 354-357; AMIDATION 293-296; CK2_PHOSPHO_SITE 20-23; CAMP_PHOSPHO_SITE 282-285; CK2_PHOSPHO_SITE 93-96; CAMP_PHOSPHO_SITE 350-353; CK2_PHOSPHO_SITE 132-135; MYRISTYL 233-238; CK2_PHOSPHO_SITE 131-134; MYRISTYL 200-205;	317; SAM_PNT 48-132; AT_hook 275-287; ETS_DOMAIN_3 304-386; SAM_PNT 48-132; HSF_ETS 314-376; ETSDOMAIN 368-386; Ets 303-388; ETS 303-390;
DEX0455_013.aa.1	N	0 - o1-219;	38-45,1.105; 183-198,1.162; 129-146,1.173; 154-173,1.144; 93-115,1.187; 4-34,1.161; 50-60,1.202;	CK2_PHOSPHO_SITE 37-40; MYRISTYL 49-54; ASN_GLYCOSYLATION 46-49; MYRISTYL 30-35; CK2_PHOSPHO_SITE 173-176; MYRISTYL 147-152; PKC_PHOSPHO_SITE 200-202; MYRISTYL 100-105; PKC_PHOSPHO_SITE 214-216;	
DEX0455_013.aa.2	N	0 - o1-172;	82-99,1.173; 4-10,1.154; 46-68,1.187; 136-151,1.162; 107-126,1.144;	CK2_PHOSPHO_SITE 126-129; MYRISTYL 100-105; MYRISTYL 53-58; PKC_PHOSPHO_SITE 167-169; PKC_PHOSPHO_SITE 153-155;	
DEX0455_014.orf.1	N	0 - o1-329;	4-10,1.104; 140-146,1.062; 76-82,1.057; 117-125,1.126; 181-192,1.181; 300-307.1.103:	CK2_PHOSPHO_SITE 110-113; CK2_PHOSPHO_SITE 24-27; CAMP_PHOSPHO_SITE 198-201; PKC_PHOSPHO_SITE 95-97; PKC_PHOSPHO_SITE 308-310; CK2_PHOSPHO_SITE 156-159; AMIDATION 12-15; CK2_PHOSPHO_SITE 177-180; PKC_PHOSPHO_SITE 204-206; MYRISTYL 29-34; CK2_PHOSPHO_SITE 210-213; PKC PHOSPHO SITE 126-128:	EFh 204-232; EF_HAND_2_1 153-229; EF_HAND 213-225; Calpain_III 1-133; EF_HAND 243-255; efhand 204-232; EFh 234-262; calpain_III 5-133: efhand

			162-169,1.103; 314-320,1.054; 52-65,1.124; 197-212,1.145; 235-242,1.069; 32-40,1.209; 96-113,1.1; 224-230,1.049; 18-24,1.096; 255-278,1.221; 290-298,1.171;	CK2_PHOSPHO_SITE 150-153; CK2_PHOSPHO_SITE 251-254; PKC_PHOSPHO_SITE 24-26; ASN_GLYCOSYLATION 299-302; CK2_PHOSPHO_SITE 22-25; MYRISTYL 248-253;	234-262; EF_HAND_2_2 237-294;
DEX0455_014.aa.1	N	0 - o1-595;	21-44,1.113; 556-564,1.171; 49-73,1.155; 75-82,1.121; 179-185,1.061; 284-290,1.096; 342-348,1.057; 117-125,1.165; 103-110,1.113; 566-573,1.103; 259-275,1.108; 428-435,1.103; 188-197,1.149; 86-98,1.077; 318-331,1.124; 447-458,1.181; 132-143,1.081; 4-11,1.247; 362-	CK2_PHOSPHO_SITE 153-156; ASN_GLYCOSYLATION 143-146; PKC_PHOSPHO_SITE 290-292; CK2_PHOSPHO_SITE 200-203; MYRISTYL 189-194; CK2_PHOSPHO_SITE 288-291; CK2_PHOSPHO_SITE 290-293; CK2_PHOSPHO_SITE 517-520; CK2_PHOSPHO_SITE 250-253; ASN_GLYCOSYLATION 17-20; MYRISTYL 295-300; PKC_PHOSPHO_SITE 392-394; ASN_GLYCOSYLATION 248-251; ASN_GLYCOSYLATION 565-568; PKC_PHOSPHO_SITE 252-254; MYRISTYL 211-216; CK2_PHOSPHO_SITE 221-224; CK2_PHOSPHO_SITE 422-425; CAMP_PHOSPHO_SITE 464-467; MYRISTYL 164-169; MYRISTYL 144-149; CK2_PHOSPHO_SITE 114-117; CK2_PHOSPHO_SITE 47-50; PKC_PHOSPHO_SITE 114-116; MYRISTYL 45-50; PKC_PHOSPHO_SITE 470-472; PKC_PHOSPHO_SITE 227-229; CK2_PHOSPHO_SITE 19-22; PKC_PHOSPHO_SITE 361-363; CK2_PHOSPHO_SITE 376-379; CK2_PHOSPHO_SITE 476-479; MYRISTYL 514-519; PKC_PHOSPHO_SITE 574-576; CK2_PHOSPHO_SITE 443-446; CK2_PHOSPHO_SITE 416-419; CAMP_PHOSPHO_SITE 187-190; TYR_PHOSPHO_SITE 172-179;	Calpain_III 261-399; THIOL_PROTEASE_CYS 53-64; EFh 470-498; CALPAIN 89-114; efhand 500-528; EF_HAND_2_1 419-495; Peptidase_C2 14-273; CYS_PROT_CALPAIN 32-273; CysPc 2-281; EF_HAND_2_2 503-560; CALPAIN 53-69; EFh 500-528; EF_HAND 509-521; CALPAIN 29-51; EF_HAND 479-491; calpain_III 241-399; CALPAIN 365-393; efhand 470-498; CALPAIN 119-142;

			379,1.1; 209-229,1.083; 490-496,1.049; 298-306,1.209; 521-544,1.221; 580-586,1.054; 463-478,1.145; 501-508,1.069; 383-391,1.126; 406-412,1.062;		
DEX0455_015.aa.1	N	0 - o1-85;	63-82,1.15; 20-26,1.04; 4-14,1.174; 35-46,1.138;	CK2_PHOSPHO_SITE 42-45; PKC_PHOSPHO_SITE 35-37; CK2_PHOSPHO_SITE 81-84; CK2_PHOSPHO_SITE 19-22; PKC_PHOSPHO_SITE 68-70;	ER_TARGET 82-85;
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DEX0455_019.aa.1	Y	0 - o1-287;	209-234,1.163; 268-274,1.108; 249-254,1.037; 171-180,1.184; 65-73,1.106; 189-197,1.098; 8-21,1.242; 91-102,1.114; 54-60,1.089; 129-136,1.123; 33-40,1.121; 236-244,1.078; 109-127,1.096; 140-154,1.114;	MYRISTYL 82-87; AMIDATION 102-105; MYRISTYL 214-219; PKC_PHOSPHO_SITE 26-28; ASN_GLYCOSYLATION 243-246; ASN_GLYCOSYLATION 163-166; PKC_PHOSPHO_SITE 238-240; PKC_PHOSPHO_SITE 193-195; MYRISTYL 247-252; CK2_PHOSPHO_SITE 218-221; PKC_PHOSPHO_SITE 165-167; ASN_GLYCOSYLATION 203-206; CK2_PHOSPHO_SITE 48-51; PKC_PHOSPHO_SITE 248-250;	Folate_rec 7-287;
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DEX0455_020.aa.2	N	0 - o1-67;	29-46,1.092; 52-64,1.187; 11-21,1.128;	CK2_PHOSPHO_SITE 44-47; ASN_GLYCOSYLATION 25-28; MYRISTYL 7-12;	
DEX0455_021.orf.1	N	0 - o1-104;	86-97,1.124; 4-9,1.11; 35-71,1.171; 14-22,1.095;	PKC_PHOSPHO_SITE 81-83; PKC_PHOSPHO_SITE 100-102; CAMP_PHOSPHO_SITE 33-36; PKC_PHOSPHO_SITE 32-34; MYRISTYL 10-15;	
DEX0455_021.aa.1	N	0 - o1-82;	45-51,1.09; 4-11,1.131; 15-23,1.096;		
DEX0455_021.aa.2	N	0 - o1-360;	112-119,1.083; 209-218,1.167; 121-147,1.118; 179-186,1.153; 73-108,1.131; 290-300,1.12; 169-175,1.09; 46-55,1.071; 309-318,1.162; 4-10,1.11; 341-347,1.071; 13-34,1.181; 193-199,1.098; 239-267,1.186;	ASN_GLYCOSYLATION 108-111; MYRISTYL 203-208; AMIDATION 217-220; CK2_PHOSPHO_SITE 44-47; AMIDATION 325-328; PKC_PHOSPHO_SITE 48-50; CK2_PHOSPHO_SITE 18-21; CAMP_PHOSPHO_SITE 78-81; PKC_PHOSPHO_SITE 56-58; MYRISTYL 263-268; MYRISTYL 190-195;	Epimerase 5-311; galE 4-296;
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			103,1.071; 61-82,1.181; 357-366,1.162; 51-58,1.11; 257-266,1.167; 169-195,1.118; 121-156,1.131; 160-167,1.083; 287-315,1.186; 338-348,1.12; 217-223,1.09; 227-234,1.153;	CAMP_PHOSPHO_SITE 126-129; MYRISTYL 238-243; CK2_PHOSPHO_SITE 66-69; MYRISTYL 9-14; AMIDATION 373-376; MYRISTYL 6-11; MYRISTYL 10-15; ASN_GLYCOSYLATION 156-159; AMIDATION 265-268; MYRISTYL 311-316; MYRISTYL 251-256;	
DEX0455_021.aa.3	N	0 - o1-466;	290-300,1.12; 239-267,1.186; 209-218,1.167; 399-417,1.182; 193-199,1.098; 4-10,1.11; 121-147,1.118; 46-55,1.071; 112-119,1.083; 337-393,1.213; 13-34,1.181; 309-318,1.162; 73-108,1.131; 169-175,1.09; 422-434,1.145; 179-186,1.153;	PKC_PHOSPHO_SITE 48-50; MYRISTYL 203-208; AMIDATION 217-220; PKC_PHOSPHO_SITE 56-58; MYRISTYL 263-268; AMIDATION 325-328; PKC_PHOSPHO_SITE 399-401; PKC_PHOSPHO_SITE 372-374; MYRISTYL 359-364; MYRISTYL 190-195; ASN_GLYCOSYLATION 108-111; PKC_PHOSPHO_SITE 346-348; CK2_PHOSPHO_SITE 44-47; CAMP_PHOSPHO_SITE 78-81; CK2_PHOSPHO_SITE 18-21;	galE 4-462; Epimerase 5-459;
DEX0455_021.aa.4	N	0 - o1-328;	112-119,1.083; 239-267,1.186; 193-	MYRISTYL 190-195; MYRISTYL 263-268; PKC_PHOSPHO_SITE 56-58; CK2_PHOSPHO_SITE 44-47; MYRISTYL 203-208; CK2 PHOSPHO SITE 18-21:	galE 4-296; Epimerase 5-311;

			199,1.098; 169-175,1.09; 309-318,1.162; 73-108,1.131; 209-218,1.167; 290-300,1.12; 121-147,1.118; 13-34,1.181; 46-55,1.071; 179-186,1.153; 4-10,1.11;	AMIDATION 217-220; ASN_GLYCOSYLATION 108-111; PKC_PHOSPHO_SITE 48-50; AMIDATION 325-328; CAMP_PHOSPHO_SITE 78-81;	
DEX0455_022.aa.1	Y	1 - i1-21;tm22-44;o45-178;	54-73,1.132; 19-46,1.26; 123-135,1.041; 5-12,1.131; 81-101,1.08; 140-149,1.16; 151-157,1.051; 161-171,1.056;	PKC_PHOSPHO_SITE 145-147; TYR_PHOSPHO_SITE 147-154; AMIDATION 173-176; CK2_PHOSPHO_SITE 4-7; ASN_GLYCOSYLATION 65-68; ASN_GLYCOSYLATION 92-95; PKC_PHOSPHO_SITE 45-47; CK2_PHOSPHO_SITE 156-159;	
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DEX0455_022.aa.2	Y	1 - i1-21;tm22-44;o45-188;	113-128,1.071; 131-144,1.136; 148-157,1.16; 19-46,1.26; 81-101,1.08; 5-12.1.131:	ASN_GLYCOSYLATION 92-95; ASN_GLYCOSYLATION 65-68; TYR_PHOSPHO_SITE 155-162; PKC_PHOSPHO_SITE 153-155; CK2_PHOSPHO_SITE 4-7; PKC_PHOSPHO_SITE 45-47; CK2_PHOSPHO_SITE 164-167;	

			169-185,1.221;159-165,1.051;54-73,1.132;		
DEX0455_022.aa.3	Y	0 - o1-78;	6-14,1.07;48-65,1.202;70-75,1.085;	MYRISTYL 48-53; MYRISTYL 34-39; MYRISTYL 14-19; MYRISTYL 27-32; MYRISTYL 6-11; PKC_PHOSPHO_SITE 68-70; MYRISTYL 39-44; MYRISTYL 13-18; MYRISTYL 20-25;	GLY_RICH 5-48;
DEX0455_023.aa.1	N	0 - o1-116;	69-80,1.147;50-61,1.08;27-37,1.085;82-89,1.049;4-13,1.11;	PKC_PHOSPHO_SITE 57-59; CAMP_PHOSPHO_SITE 48-51; PKC_PHOSPHO_SITE 52-54; PKC_PHOSPHO_SITE 47-49; PKC_PHOSPHO_SITE 101-103; PKC_PHOSPHO_SITE 43-45; CK2_PHOSPHO_SITE 36-39; AMIDATION 39-42; PKC_PHOSPHO_SITE 97-99; CAMP_PHOSPHO_SITE 54-57;	
DEX0455_024.aa.1	N	0 - o1-360;	245-252,1.15;127-136,1.145;208-215,1.12;309-317,1.126;117-124,1.107;274-284,1.206;189-197,1.193;348-357,1.265;324-340,1.091;147-157,1.162;78-85,1.168;232-240,1.187;167-172,1.042;289-295,1.073;61-70,1.189;	PKC_PHOSPHO_SITE 34-36; PKC_PHOSPHO_SITE 257-259; PKC_PHOSPHO_SITE 33-35; PKC_PHOSPHO_SITE 298-300; MYRISTYL 6-11; MYRISTYL 144-149; CK2_PHOSPHO_SITE 176-179; ASN_GLYCOSYLATION 286-289; PKC_PHOSPHO_SITE 22-24; CAMP_PHOSPHO_SITE 254-257; MYRISTYL 29-34; PKC_PHOSPHO_SITE 7-9; CK2_PHOSPHO_SITE 344-347; CK2_PHOSPHO_SITE 315-318; CK2_PHOSPHO_SITE 272-275; CAMP_PHOSPHO_SITE 163-166; CK2_PHOSPHO_SITE 71-74; MYRISTYL 303-308; CK2_PHOSPHO_SITE 158-161; PKC_PHOSPHO_SITE 264-266; CK2_PHOSPHO_SITE 73-76; CK2_PHOSPHO_SITE 257-260;	ANNEXINI 343-356; sp_P09525_ANX4_HUMAN 131-196; ANNEXINV 219-245; annexin 212-280; ANNEXINV 343-356; ANNEXINV 136-157; annexin 288-355; ANNEXIN 109-125; sp_P08132_ANX4_PIG 214-283; ANNEXIN 136-157; sp_Q9NFS4_Q9NFS4_GIALA 89-348; ANNEXIN 219-245; ANNEXINV 299-325; ANNEXIN 72-124; ANNEXINI 299-319; ANNEXINI 219-245; annexin 16-124; ANNEXIN 228-280; ANNEXINI 136-157; annexin 129-196; ANX 303-355; ANNEXINV 69-91; ANX 144-196; ANNEXINI 69-91;

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			564,1.066; 111-121,1.127; 9-15,1.13; 655-665,1.082; 243-250,1.061; 73-90,1.133; 507-513,1.056; 124-165,1.203; 539-548,1.107; 623-630,1.089; 253-265,1.112; 360-365,1.048; 280-315,1.154; 386-392,1.069; 394-416,1.152; 489-499,1.139; 269-278,1.061; 368-384,1.143; 578-589,1.155; 175-185,1.225; 473-482,1.179; 201-211,1.092; 323-355,1.122; 25-49,1.169; 424-465,1.143; 55-61,1.085; 633-639,1.052; 601-618,1.106; 521-528,1.118;	MYRISTYL 224-229; PKC_PHOSPHO_SITE 632-634; CK2_PHOSPHO_SITE 653-656; CK2_PHOSPHO_SITE 228-231; MYRISTYL 349-354; CK2_PHOSPHO_SITE 230-233; MYRISTYL 507-512; MYRISTYL 361-366; PKC_PHOSPHO_SITE 588-590; CK2_PHOSPHO_SITE 640-643; PKC_PHOSPHO_SITE 526-528; MYRISTYL 55-60; PKC_PHOSPHO_SITE 555-557; CK2_PHOSPHO_SITE 118-121; PKC_PHOSPHO_SITE 71-73; LEUCINE_ZIPPER 453-474; PKC_PHOSPHO_SITE 631-633; PKC_PHOSPHO_SITE 68-70; CK2_PHOSPHO_SITE 540-543; PKC_PHOSPHO_SITE 513-515; ASN_GLYCOSYLATION 51-54; MYRISTYL 674-679; CK2_PHOSPHO_SITE 318-321; CK2_PHOSPHO_SITE 308-311; CK2_PHOSPHO_SITE 169-172;	
DEX0455_026.orf.1	N	0 - i1-72;		ASN_GLYCOSYLATION 46-49; CK2_PHOSPHO_SITE 62-65;	

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DEX0455_027.orf.1	N	0 - o1-174;	54-76,1.16; 118-139,1.134; 40-52,1.162; 4-20,1.164; 155-171,1.137; 103-113,1.167;	CK2_PHOSPHO_SITE 65-68; MYRISTYL 53-58; MYRISTYL 40-45; PKC_PHOSPHO_SITE 75-77; ASN_GLYCOSYLATION 93-96; CK2_PHOSPHO_SITE 171-174; CK2_PHOSPHO_SITE 114-117; CK2_PHOSPHO_SITE 83-86; MYRISTYL 152-157;	
DEX0455_027.aa.1	N	0 - i1-36;	5-28,1.145;		
DEX0455_028.aa.1	N	0 - o1-215;		MYRISTYL 144-149; CK2_PHOSPHO_SITE 30-33; PKC_PHOSPHO_SITE 111-113; PKC_PHOSPHO_SITE 68-70; CK2_PHOSPHO_SITE 111-114; MYRISTYL 52-57; CK2_PHOSPHO_SITE 167-170; CK2_PHOSPHO_SITE 28-31; GLYCOSAMINOGLYCAN 36-39; MYRISTYL 106-111; CK2_PHOSPHO_SITE 7-10; PKC_PHOSPHO_SITE 210-212; CK2_PHOSPHO_SITE 82-85;	cobW 41-214; ATP_GTP_A 49-56;
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.3		71;tm72-94;i95-101;	61-81,1.213; 83-98,1.241; 4-12,1.132;	99-101;	
DEX0455_036.orf.1	N	1 - o1-40;tm41-63;i64-95;	39-66,1.248; 76-92,1.111; 15-24,1.133;	TYR_PHOSPHO_SITE 68-75; PKC_PHOSPHO_SITE 66-68; MYRISTYL 61-66; CK2_PHOSPHO_SITE 87-90; PKC_PHOSPHO_SITE 65-67; ASN_GLYCOSYLATION 11-14; MYRISTYL 53-58;	
DEX0455_036.aa.1	N	1 - o1-54;tm55-77;i78-109;	53-80,1.248; 4-16,1.142; 29-38,1.133; 90-106,1.111;	TYR_PHOSPHO_SITE 82-89; MYRISTYL 75-80; CK2_PHOSPHO_SITE 101-104; PKC_PHOSPHO_SITE 80-82; MYRISTYL 67-72; ASN_GLYCOSYLATION 25-28; PKC_PHOSPHO_SITE 79-81; MYRISTYL 10-15;	G_PROTEIN_RECEP_F1_1 18-34;
DEX0455_036.aa.2	N	0 - o1-1485;	427-433,1.051; 715-725,1.093; 1161-1180,1.113; 1009-1017,1.062; 1369-1374,1.054; 1428-1480,1.146; 673-683,1.16; 594-600,1.049; 170-199,1.136; 1388-1401,1.161; 126-132,1.062; 809-823,1.119; 405-413,1.091; 104-110,1.07; 480-511,1.148; 1405-1417,1.159; 1356-1366,1.086; 895-901,1.051; 49-61.1.148:	PKC_PHOSPHO_SITE 1000-1002; MYRISTYL 191-196; CK2_PHOSPHO_SITE 440-443; ASN_GLYCOSYLATION 338-341; TYR_PHOSPHO_SITE 237-245; CK2_PHOSPHO_SITE 986-989; ASN_GLYCOSYLATION 806-809; PKC_PHOSPHO_SITE 1415-1417; ASN_GLYCOSYLATION 1385-1388; MYRISTYL 35-40; PKC_PHOSPHO_SITE 837-839; ASN_GLYCOSYLATION 478-481; PKC_PHOSPHO_SITE 1148-1150; CK2_PHOSPHO_SITE 82-85; MYRISTYL 124-129; PKC_PHOSPHO_SITE 525-527; ASN_GLYCOSYLATION 457-460; MYRISTYL 436-441; PKC_PHOSPHO_SITE 318-320; CK2_PHOSPHO_SITE 550-553; CK2_PHOSPHO_SITE 1275-1278; CK2_PHOSPHO_SITE 50-53; CK2_PHOSPHO_SITE 362-365; PKC_PHOSPHO_SITE 102-104; CK2_PHOSPHO_SITE 674-677; MYRISTYL 47-52; ASN_GLYCOSYLATION 790-793; ASN_GLYCOSYLATION 1235-1238; ASN_GLYCOSYLATION 1365-1368; PKC_PHOSPHO_SITE 681-683; CK2_PHOSPHO_SITE 862-865; ASN_GLYCOSYLATION 1029-1032; PKC_PHOSPHO_SITE 1038-1040; MYRISTYL 659-664; ASN_GLYCOSYLATION 634-637; PKC_PHOSPHO_SITE 636-638; ASN_GLYCOSYLATION	SEA_1 757-823; SEA_2 913-979;

			73-89,1.07; 114-121,1.085; 14-43,1.136; 416-422,1.032; 1195-1210,1.091; 873-880,1.078; 341-355,1.139; 1061-1081,1.165; 1051-1059,1.101; 135-145,1.171; 572-578,1.043; 537-557,1.079; 603-620,1.171; 1341-1351,1.091; 742-747,1.017; 1276-1305,1.178; 1022-1027,1.076; 853-869,1.079; 987-998,1.127; 750-756,1.049; 1241-1253,1.146; 260-266,1.074; 561-568,1.078; 517-527,1.127; 583-589,1.035; 1255-1269,1.16; 437-443,1.069; 361-374,1.127; 649-667,1.12; 1120-	1081-1084; MYRISTYL 1126-1131; MYRISTYL 954-959; CK2_PHOSPHO_SITE 206-209; PKC_PHOSPHO_SITE 1103-1105; ASN_GLYCOSYLATION 650-653; CK2_PHOSPHO_SITE 518-521; PKC_PHOSPHO_SITE 258-260; PKC_PHOSPHO_SITE 1097-1099; ASN_GLYCOSYLATION 1117-1120; MYRISTYL 983-988; ASN_GLYCOSYLATION 1101-1104; ASN_GLYCOSYLATION 769-772; ASN_GLYCOSYLATION 301-304; MYRISTYL 503-508; ASN_GLYCOSYLATION 1018-1021; ASN_GLYCOSYLATION 322-325; ASN_GLYCOSYLATION 925-928; PKC_PHOSPHO_SITE 746-748; ASN_GLYCOSYLATION 613-616; PKC_PHOSPHO_SITE 948-950; PKC_PHOSPHO_SITE 786-788; CK2_PHOSPHO_SITE 830-833; PKC_PHOSPHO_SITE 162-164; MYRISTYL 1255-1260; PKC_PHOSPHO_SITE 347-349; PKC_PHOSPHO_SITE 882-884; PKC_PHOSPHO_SITE 942-944; MYRISTYL 203-208; MYRISTYL 971-976; PKC_PHOSPHO_SITE 324-326; ASN_GLYCOSYLATION 946-949; PKC_PHOSPHO_SITE 792-794; CK2_PHOSPHO_SITE 1173-1176; PKC_PHOSPHO_SITE 570-572; PKC_PHOSPHO_SITE 733-735; PKC_PHOSPHO_SITE 1268-1270; MYRISTYL 1227-1232; MYRISTYL 904-909; PKC_PHOSPHO_SITE 213-215; PKC_PHOSPHO_SITE 1337-1339; PKC_PHOSPHO_SITE 1231-1233; TYR_PHOSPHO_SITE 1002-1009; PKC_PHOSPHO_SITE 168-170; MYRISTYL 815-820; ASN_GLYCOSYLATION 166-169; PKC_PHOSPHO_SITE 474-476; CK2_PHOSPHO_SITE 1425-1428; MYRISTYL 1426-1431; CK2_PHOSPHO_SITE 1141-1144; ASN_GLYCOSYLATION 10-13; ASN_GLYCOSYLATION 1214-1217; PKC_PHOSPHO_SITE 57-59; PKC_PHOSPHO_SITE 630-632; PKC_PHOSPHO_SITE 12-14; MYRISTYL 1422-1427; PKC_PHOSPHO_SITE 1193-	

			1134,1.119; 759-769,1.186; 1142-1150,1.127; 1311-1324,1.069; 448-457,1.171; 205-221,1.105; 1029-1037,1.068; 529-535,1.029; 950-979,1.128; 229-257,1.102; 904-925,1.198; 271-277,1.063; 697-708,1.073; 326-335,1.128; 1105-1114,1.128; 794-806,1.128; 93-101,1.078; 385-396,1.062; 829-839,1.135; 1040-1046,1.055; 884-890,1.07; 1184-1192,1.078; 638-647,1.128; 282-301,1.181;	1195; ASN_GLYCOSYLATION 145-148; PKC_PHOSPHO_SITE 6-8;	
DEX0455_036.orf.3	N	1 - o1-56;tm57-79;i80-111;		MYRISTYL 12-17; PKC_PHOSPHO_SITE 81-83; CK2_PHOSPHO_SITE 103-106; TYR_PHOSPHO_SITE 84-91; ASN_GLYCOSYLATION 11-14; PKC_PHOSPHO_SITE 82-84; MYRISTYL 69-74; MYRISTYL 11-16; ASN_GLYCOSYLATION 10-13; TYR_PHOSPHO_SITE 6-12; MYRISTYL 77-82;	
DEX0455_036.aa	N	1 - o1-	8-16,1.19; 68-	MYRISTYL 53-58; TYR_PHOSPHO_SITE 60-67;	

.3		32;tm33-55;i56-87;	84,1.111; 31-58,1.248;	CK2_PHOSPHO_SITE 79-82; PKC_PHOSPHO_SITE 58-60; MYRISTYL 45-50; PKC_PHOSPHO_SITE 57-59;	
DEX0455_036.orf.4	N	0 - o1-92;	20-29,1.064; 41-53,1.181; 62-72,1.212; 4-10,1.151;	AMIDATION 34-37; PKC_PHOSPHO_SITE 51-53; MYRISTYL 56-61; PKC_PHOSPHO_SITE 88-90; PKC_PHOSPHO_SITE 62-64; MYRISTYL 61-66;	
DEX0455_036.aa.4	N	1 - o1-28;tm29-51;i52-83;	64-80,1.111; 27-54,1.248; 4-13,1.104;	PKC_PHOSPHO_SITE 54-56; MYRISTYL 49-54; MYRISTYL 41-46; CK2_PHOSPHO_SITE 75-78; PKC_PHOSPHO_SITE 53-55; TYR_PHOSPHO_SITE 56-63;	
DEX0455_037.aa.1	Y	0 - o1-225;	199-205,1.08; 60-72,1.178; 150-159,1.178; 161-169,1.13; 116-126,1.06; 181-186,1.025; 45-52,1.052; 8-33,1.189; 210-219,1.123; 137-143,1.07; 94-108,1.076;	MYRISTYL 124-129; CK2_PHOSPHO_SITE 154-157; PKC_PHOSPHO_SITE 189-191; PKC_PHOSPHO_SITE 106-108; CK2_PHOSPHO_SITE 109-112; MYRISTYL 129-134; ASN_GLYCOSYLATION 78-81; PKC_PHOSPHO_SITE 109-111; MYRISTYL 144-149; CK2_PHOSPHO_SITE 158-161; MYRISTYL 100-105; MYRISTYL 133-138; ASN_GLYCOSYLATION 51-54; MYRISTYL 76-81; MYRISTYL 148-153; PKC_PHOSPHO_SITE 218-220; MYRISTYL 47-52;	PGNDSYNTHASE 74-92; PGNDSYNTHASE 31-54; PGNDSYNTHASE 57-67; LIPOCALIN 33-46; lipocalin 38-221;
DEX0455_037.orf.2	N	0 - o1-349;	294-307,1.148; 108-114,1.075; 200-209,1.156; 320-335,1.295; 263-275,1.199; 15-38,1.169; 246-252,1.033; 6-12,1.064; 87-93.1.037:	PKC_PHOSPHO_SITE 215-217; PKC_PHOSPHO_SITE 173-175; MYRISTYL 185-190; AMIDATION 123-126; PKC_PHOSPHO_SITE 4-6; MYRISTYL 190-195; CAMP_PHOSPHO_SITE 228-231; PKC_PHOSPHO_SITE 179-181; MYRISTYL 223-228; MYRISTYL 116-121; PKC_PHOSPHO_SITE 83-85; PKC_PHOSPHO_SITE 226-228; CK2_PHOSPHO_SITE 256-259; PKC_PHOSPHO_SITE 120-122; AMIDATION 226-229; PKC_PHOSPHO_SITE 243-245; PKC_PHOSPHO_SITE 105-107; MYRISTYL 283-288; MYRISTYL 287-292:	PRICHEXTENSN 247-263; PRICHEXTENSN 172-184; PRICHEXTENSN 339-349; PRICHEXTENSN 148-164;

			237-242,1.056; 45-70,1.189; 132-149,1.075; 97-102,1.067; 338-346,1.088; 159-172,1.15; 309-315,1.106; 219-225,1.098;	PKC_PHOSPHO_SITE 95-97; MYRISTYL 195-200; MYRISTYL 193-198; MYRISTYL 288-293; MYRISTYL 275-280; MYRISTYL 285-290; CAMP_PHOSPHO_SITE 1-4; MYRISTYL 99-104;	
DEX0455_037.aa.2	Y	0 - o1-413;	369-374,1.025; 283-295,1.178; 349-357,1.13; 338-347,1.178; 50-56,1.037; 268-275,1.052; 387-393,1.08; 193-201,1.082; 317-332,1.076; 218-224,1.049; 231-240,1.065; 60-65,1.067; 71-77,1.075; 129-135,1.033; 8-33,1.189; 141-148,1.121; 95-113,1.107; 398-407,1.123;	PKC_PHOSPHO_SITE 83-85; MYRISTYL 270-275; PKC_PHOSPHO_SITE 329-331; MYRISTYL 62-67; MYRISTYL 236-241; MYRISTYL 171-176; PKC_PHOSPHO_SITE 406-408; AMIDATION 256-259; MYRISTYL 154-159; MYRISTYL 168-173; AMIDATION 86-89; MYRISTYL 190-195; CK2_PHOSPHO_SITE 342-345; PKC_PHOSPHO_SITE 216-218; MYRISTYL 336-341; MYRISTYL 186-191; CK2_PHOSPHO_SITE 346-349; ASN_GLYCOSYLATION 301-304; PKC_PHOSPHO_SITE 162-164; CK2_PHOSPHO_SITE 177-180; MYRISTYL 256-261; MYRISTYL 323-328; ASN_GLYCOSYLATION 274-277; MYRISTYL 170-175; PKC_PHOSPHO_SITE 377-379; PKC_PHOSPHO_SITE 58-60; MYRISTYL 299-304; ASN_GLYCOSYLATION 226-229; MYRISTYL 79-84; PKC_PHOSPHO_SITE 46-48; PKC_PHOSPHO_SITE 68-70;	LIPOCALIN 256-269; A1MCGLOBULIN 269-280; lipocalin 261-409; MAJORURINARY 263-281; VNEBNERGLAND 300-312; PGNDSYNTHASE 368-382; VNEBNERGLAND 371-394; LIPOCALIN 343-355; LIPOCALIN 260-272; VNEBNERGLAND 260-274; PGNDSYNTHASE 385-403; LIPOCALIN 371-386; A1MCGLOBULIN 366-387; MAJORURINARY 393-410; A1MCGLOBULIN 394-413; PGNDSYNTHASE 280-290; MAJORURINARY 365-386; PGNDSYNTHASE 332-355; A1MCGLOBULIN 334-353; PGNDSYNTHASE 254-277; PGNDSYNTHASE 297-315;
DEX0455 037.aa	Y	0 - o1-	95-112.1.075:	MYRISTYL 304-309; MYRISTYL 251-256: MYRISTYL 336-341:	GLY_RICH 236-395;

.3		410;	209-215,1.033; 163-172,1.156; 200-205,1.056; 60-65,1.067; 292-298,1.068; 370-376,1.106; 381-396,1.295; 50-56,1.037; 226-238,1.199; 281-288,1.078; 122-135,1.15; 71-77,1.075; 345-351,1.103; 8-33,1.189; 182-188,1.098; 308-317,1.074; 399-407,1.088; 360-368,1.106;	MYRISTYL 264-269; AMIDATION 285-288; MYRISTYL 148-153; CAMP_PHOSPHO_SITE 191-194; MYRISTYL 282-287; MYRISTYL 156-161; MYRISTYL 153-158; AMIDATION 189-192; PKC_PHOSPHO_SITE 189-191; MYRISTYL 250-255; PKC_PHOSPHO_SITE 136-138; PKC_PHOSPHO_SITE 142-144; MYRISTYL 299-304; AMIDATION 86-89; MYRISTYL 238-243; PKC_PHOSPHO_SITE 178-180; PKC_PHOSPHO_SITE 58-60; MYRISTYL 330-335; AMIDATION 339-342; MYRISTYL 79-84; PKC_PHOSPHO_SITE 68-70; MYRISTYL 186-191; MYRISTYL 318-323; PKC_PHOSPHO_SITE 206-208; CK2_PHOSPHO_SITE 219-222; MYRISTYL 322-327; MYRISTYL 274-279; PKC_PHOSPHO_SITE 83-85; MYRISTYL 248-253; MYRISTYL 246-251; PKC_PHOSPHO_SITE 46-48; MYRISTYL 158-163; MYRISTYL 326-331; MYRISTYL 62-67;	
DEX0455_037.aa.4	Y	0 - o1-135;	38-44,1.052; 8-36,1.181; 109-115,1.08; 46-89,1.223; 120-129,1.123;	MYRISTYL 71-76; PKC_PHOSPHO_SITE 99-101; MYRISTYL 54-59; ASN_GLYCOSYLATION 93-96; MYRISTYL 21-26; PKC_PHOSPHO_SITE 128-130;	PGNDSYNTHASE 90-104; PGNDSYNTHASE 107-125;
DEX0455_037.aa.5	N	0 - o1-150;	110-116,1.09; 11-27,1.137; 75-102,1.154; 137-147,1.065; 47-53,1.067; 38-45,1.081;	MYRISTYL 62-67; MYRISTYL 51-56; ASN_GLYCOSYLATION 71-74; PKC_PHOSPHO_SITE 33-35; MYRISTYL 74-79; MYRISTYL 138-143; MYRISTYL 65-70; MYRISTYL 69-74; PKC_PHOSPHO_SITE 116-118; MYRISTYL 115-120; MYRISTYL 105-110; CK2_PHOSPHO_SITE 46-49;	
DEX0455	Y	0 -	149-	MYRISTYL 100-105; MYRISTYL	LIPOCALIN 33-

_037.aa .6		o1- 224;	158,1.178; 137- 143,1.07; 209- 218,1.123; 116- 126,1.06; 198- 204,1.08; 45- 52,1.052; 94- 108,1.076; 160- 168,1.13; 8- 33,1.189; 60- 72,1.178; 180- 185,1.025;	147-152; PKC_PHOSPHO_SITE 188-190; MYRISTYL 47-52; ASN_GLYCOSYLATION 51-54; MYRISTYL 124-129; PKC_PHOSPHO_SITE 106-108; CK2_PHOSPHO_SITE 109-112; MYRISTYL 129-134; CK2_PHOSPHO_SITE 153-156; ASN_GLYCOSYLATION 78-81; MYRISTYL 133-138; PKC_PHOSPHO_SITE 109-111; CK2_PHOSPHO_SITE 157-160; MYRISTYL 76-81; PKC_PHOSPHO_SITE 217-219;	46; lipocalin 38-220; PGNDSYNTHASE 31-54; PGNDSYNTHASE 57-67; PGNDSYNTHASE 74-92;
DEX0455 _037.aa .7	Y	0 - o1- 481;	458- 464,1.07; 281- 288,1.078; 381- 393,1.178; 122- 135,1.15; 358- 364,1.026; 308- 317,1.074; 226- 238,1.199; 71- 77,1.075; 200- 205,1.056; 345- 351,1.103; 209- 215,1.033; 163- 172,1.156; 182- 188,1.098; 292- 298,1.068; 60- 65,1.067; 415- 429,1.076; 50- 56,1.037; 95- 112,1.075; 366- 373.1.052:	MYRISTYL 156-161; MYRISTYL 336-341; PKC_PHOSPHO_SITE 58-60; PKC_PHOSPHO_SITE 68-70; MYRISTYL 79-84; CK2_PHOSPHO_SITE 430-433; MYRISTYL 282-287; MYRISTYL 264-269; AMIDATION 285- 288; MYRISTYL 445-450; MYRISTYL 330-335; MYRISTYL 318-323; PKC_PHOSPHO_SITE 46-48; PKC_PHOSPHO_SITE 136-138; PKC_PHOSPHO_SITE 83-85; ASN_GLYCOSYLATION 399-402; MYRISTYL 186-191; MYRISTYL 450-455; MYRISTYL 299-304; MYRISTYL 421-426; CAMP_PHOSPHO_SITE 191-194; MYRISTYL 454-459; MYRISTYL 238-243; PKC_PHOSPHO_SITE 427-429; MYRISTYL 62-67; PKC_PHOSPHO_SITE 206-208; MYRISTYL 246-251; AMIDATION 86-89; MYRISTYL 274-279; PKC_PHOSPHO_SITE 189-191; MYRISTYL 397-402; MYRISTYL 368-373; MYRISTYL 468-473; MYRISTYL 158-163; PKC_PHOSPHO_SITE 142-144; MYRISTYL 148-153; ASN_GLYCOSYLATION 372-375; CK2_PHOSPHO_SITE 219-222; MYRISTYL 304-309; MYRISTYL 250-255; MYRISTYL 251-256; PKC_PHOSPHO_SITE 472-474; MYRISTYL 322-327; MYRISTYL 153-158; AMIDATION 339- 342; MYRISTYL 326-331; MYRISTYL 248-253:	LIPOCALIN 354- 367; PGNDSYNTHASE 395-413; PGNDSYNTHASE 352-375; GLY_RICH 236- 355; PGNDSYNTHASE 378-388;

			8-33,1.189; 437-447,1.06;	PKC_PHOSPHO_SITE 178-180; PKC_PHOSPHO_SITE 430-432; AMIDATION 189-192;	
DEX0455_038.aa.1	N	1 - i1-8;tm9-31;o32-1088;	605-611,1.066; 944-955,1.104; 810-816,1.069; 542-551,1.102; 674-692,1.106; 879-897,1.086; 765-778,1.082; 1006-1012,1.077; 518-531,1.078; 856-863,1.092; 462-468,1.065; 174-186,1.219; 1080-1085,1.064; 822-829,1.06; 144-172,1.186; 565-571,1.09; 841-849,1.057; 712-722,1.142; 731-752,1.127; 130-135,1.037; 661-667,1.036; 89-127,1.18; 1039-1050,1.161; 904-911,1.142; 957-964,1.055; 1017-1027,1.15; 973-986,1.075; 915-	AMIDATION 268-271; CK2_PHOSPHO_SITE 423-426; AMIDATION 278-281; AMIDATION 288-291; PKC_PHOSPHO_SITE 750-752; CAMP_PHOSPHO_SITE 476-479; PKC_PHOSPHO_SITE 722-724; CK2_PHOSPHO_SITE 632-635; PKC_PHOSPHO_SITE 164-166; AMIDATION 248-251; PKC_PHOSPHO_SITE 209-211; AMIDATION 338-341; PKC_PHOSPHO_SITE 525-527; PKC_PHOSPHO_SITE 481-483; CK2_PHOSPHO_SITE 781-784; PKC_PHOSPHO_SITE 32-34; CK2_PHOSPHO_SITE 135-138; ASN_GLYCOSYLATION 931-934; CK2_PHOSPHO_SITE 998-1001; AMIDATION 228-231; AMIDATION 318-321; CK2_PHOSPHO_SITE 1059-1062; AMIDATION 238-241; CK2_PHOSPHO_SITE 37-40; CK2_PHOSPHO_SITE 847-850; CK2_PHOSPHO_SITE 408-411; PKC_PHOSPHO_SITE 135-137; AMIDATION 308-311; AMIDATION 436-439; AMIDATION 396-399; PKC_PHOSPHO_SITE 539-541; AMIDATION 416-419; CK2_PHOSPHO_SITE 615-618; CK2_PHOSPHO_SITE 722-725; AMIDATION 426-429; PKC_PHOSPHO_SITE 615-617; MYRISTYL 186-191; AMIDATION 446-449; PKC_PHOSPHO_SITE 804-806; PKC_PHOSPHO_SITE 72-74; AMIDATION 368-371; CK2_PHOSPHO_SITE 775-778; CK2_PHOSPHO_SITE 561-564; CK2_PHOSPHO_SITE 828-831; AMIDATION 218-221; AMIDATION 376-379; PKC_PHOSPHO_SITE 902-904; MYRISTYL 189-194; CK2_PHOSPHO_SITE 32-35; CK2_PHOSPHO_SITE 664-667; ASN_GLYCOSYLATION 207-210; CK2_PHOSPHO_SITE 36-39; AMIDATION 386-389; AMIDATION 198-201; AMIDATION 328-331:	TROPOMYOSIN 622-639; TROPOMYOSIN 695-715; Rib_recp_KP_reg 33-176; LYS_RICH 47-82; TROPOMYOSIN 764-787; TROPOMYOSIN 831-856;

			930,1.17; 780-793,1.075; 493-510,1.135; 8-31,1.182; 594-602,1.136; 616-631,1.118;	MYRISTYL 195-200; PKC_PHOSPHO_SITE 1070-1072; AMIDATION 348-351; AMIDATION 258-261; ASN_GLYCOSYLATION 91-94; PKC_PHOSPHO_SITE 1027-1029; MYRISTYL 1031-1036;	
DEX0455_038.orf.3	N	1 - i1-107;tm108-130;o131-440;	49-58,1.131; 243-271,1.186; 188-226,1.18; 107-130,1.182; 16-27,1.089; 64-96,1.129; 229-234,1.037; 273-285,1.219;	PKC_PHOSPHO_SITE 263-265; AMIDATION 357-360; PKC_PHOSPHO_SITE 234-236; AMIDATION 297-300; AMIDATION 377-380; AMIDATION 327-330; CK2_PHOSPHO_SITE 136-139; CK2_PHOSPHO_SITE 234-237; PKC_PHOSPHO_SITE 308-310; AMIDATION 427-430; CK2_PHOSPHO_SITE 135-138; AMIDATION 317-320; AMIDATION 39-42; MYRISTYL 70-75; AMIDATION 347-350; AMIDATION 417-420; MYRISTYL 285-290; MYRISTYL 294-299; ASN_GLYCOSYLATION 190-193; MYRISTYL 7-12; CK2_PHOSPHO_SITE 131-134; AMIDATION 43-46; PKC_PHOSPHO_SITE 131-133; AMIDATION 367-370; PKC_PHOSPHO_SITE 32-34; AMIDATION 387-390; PKC_PHOSPHO_SITE 59-61; PKC_PHOSPHO_SITE 171-173; ASN_GLYCOSYLATION 306-309; AMIDATION 407-410; AMIDATION 337-340; MYRISTYL 288-293;	LYS_RICH 146-181; Rib_recp_KP_reg 132-275;
DEX0455_038.aa.3	Y	1 - i1-8;tm9-31;o32-521;	174-186,1.219; 415-423,1.129; 130-135,1.037; 396-413,1.186; 8-31,1.182; 144-172,1.186; 339-377,1.18; 455-464,1.102; 507-515,1.136;	ASN_GLYCOSYLATION 91-94; MYRISTYL 417-422; MYRISTYL 189-194; PKC_PHOSPHO_SITE 438-440; PKC_PHOSPHO_SITE 452-454; MYRISTYL 186-191; PKC_PHOSPHO_SITE 135-137; AMIDATION 228-231; PKC_PHOSPHO_SITE 209-211; AMIDATION 238-241; PKC_PHOSPHO_SITE 519-521; AMIDATION 198-201; PKC_PHOSPHO_SITE 164-166; CK2_PHOSPHO_SITE 32-35; AMIDATION 248-251; PKC_PHOSPHO_SITE 385-387; AMIDATION 258-261; MYRISTYL 195-200; CK2_PHOSPHO_SITE 135-138;	Rib_recp_KP_reg 278-426; LYS_RICH 47-82; Rib_recp_KP_reg 33-176;

			478-484,1.09; 431-444,1.078; 380-385,1.037; 89-127,1.18;	AMIDATION 278-281; PKC_PHOSPHO_SITE 72-74; AMIDATION 308-311; CK2_PHOSPHO_SITE 474-477; CK2_PHOSPHO_SITE 413-416; AMIDATION 218-221; PKC_PHOSPHO_SITE 32-34; AMIDATION 318-321; CK2_PHOSPHO_SITE 385-388; AMIDATION 288-291; AMIDATION 268-271; CK2_PHOSPHO_SITE 37-40; AMIDATION 328-331; CK2_PHOSPHO_SITE 36-39; ASN_GLYCOSYLATION 207-210;	
DEX0455_039.aa.1	Y	0 - o1-165;	53-71,1.107; 74-80,1.034; 86-93,1.108; 6-30,1.126; 34-40,1.082; 125-132,1.062;	PKC_PHOSPHO_SITE 72-74; MYRISTYL 41-46; MYRISTYL 78-83; CK2_PHOSPHO_SITE 110-113; AMIDATION 157-160; PKC_PHOSPHO_SITE 3-5; CK2_PHOSPHO_SITE 121-124; MYRISTYL 76-81; CK2_PHOSPHO_SITE 117-120; CK2_PHOSPHO_SITE 119-122; CK2_PHOSPHO_SITE 32-35; AMIDATION 152-155; CK2_PHOSPHO_SITE 66-69; MYRISTYL 45-50;	LYS_RICH 141-161;
DEX0455_039.aa.2	N	0 - o1-262;	103-113,1.095; 74-80,1.034; 210-229,1.107; 6-30,1.126; 118-132,1.11; 86-93,1.108; 53-71,1.107; 139-168,1.129; 174-207,1.173; 34-40,1.082;	MYRISTYL 76-81; AMIDATION 254-257; MYRISTYL 112-117; PKC_PHOSPHO_SITE 3-5; CK2_PHOSPHO_SITE 66-69; AMIDATION 249-252; MYRISTYL 41-46; MYRISTYL 173-178; MYRISTYL 45-50; PKC_PHOSPHO_SITE 72-74; CK2_PHOSPHO_SITE 32-35; MYRISTYL 78-83;	LYS_RICH 238-258;
DEX0455_040.orf.1	Y	0 - o1-231;		CK2_PHOSPHO_SITE 51-54; MYRISTYL 88-93; CK2_PHOSPHO_SITE 98-101; RGD 219-221; PKC_PHOSPHO_SITE 223-225; CK2_PHOSPHO_SITE 108-111; MYRISTYL 91-96; PKC_PHOSPHO_SITE 190-192; MYRISTYL 183-188; MYRISTYL 212-217; MYRISTYL 42-47; MYRISTYL 204-209;	BPTI_KUNITZ_2_1 56-106; BASICPTASE 53-67; BPTI_KUNITZ_1 179-197; KU 54-107; BASICPTASE 91-106; sp_043291_SPT2_HUMAN 56-106; sp_043291_SPT2

				ASN_GLYCOSYLATION 112-115; MYRISTYL 186-191; MYRISTYL 216-221; ASN_GLYCOSYLATION 75-78; MYRISTYL 24-29; MYRISTYL 182-187; PKC_PHOSPHO_SITE 119-121; MYRISTYL 87-92;	HUMAN 151-201; Kunitz_BPTI 151-201; KU 149-202; Kunitz_BPTI 56-106; BASICPTASE 81-91; BPTI_KUNITZ_2_2 151-201; BPTI_KUNITZ_1 84-102;
DEX0455_040.aa.1	Y	0 - o1-213;	60-70,1.189; 107-113,1.087; 147-153,1.047; 178-188,1.133; 81-91,1.13; 130-136,1.11; 10-28,1.181; 138-145,1.083; 35-47,1.25;	MYRISTYL 69-74; CK2_PHOSPHO_SITE 80-83; MYRISTYL 195-200; MYRISTYL 207-212; PKC_PHOSPHO_SITE 204-206; CK2_PHOSPHO_SITE 90-93; MYRISTYL 70-75; MYRISTYL 73-78; MYRISTYL 203-208; MYRISTYL 168-173; ASN_GLYCOSYLATION 94-97; ASN_GLYCOSYLATION 57-60; PKC_PHOSPHO_SITE 172-174; MYRISTYL 6-11; MYRISTYL 165-170; PKC_PHOSPHO_SITE 101-103; MYRISTYL 198-203; MYRISTYL 164-169; CK2_PHOSPHO_SITE 33-36; MYRISTYL 24-29;	KU 131-184; Kunitz_BPTI 38-88; BASICPTASE 35-49; sp_O43291_SPT2_HUMAN 133-183; BPTI_KUNITZ_1 66-84; BPTI_KUNITZ_2_2 133-183; BPTI_KUNITZ_1 161-179; BASICPTASE 73-88; Kunitz_BPTI 133-183; BPTI_KUNITZ_2_1 38-88; KU 36-89; sp_O43291_SPT2_HUMAN 38-88; BASICPTASE 63-73;
DEX0455_040.aa.2	Y	0 - o1-242;	35-47,1.25; 107-113,1.087; 201-239,1.186; 178-186,1.133; 130-136,1.11; 138-145,1.083; 189-195,1.083; 10-28,1.181; 81-91,1.13; 60-70,1.189; 147-153,1.047;	MYRISTYL 73-78; MYRISTYL 6-11; MYRISTYL 168-173; ASN_GLYCOSYLATION 94-97; CK2_PHOSPHO_SITE 33-36; PKC_PHOSPHO_SITE 172-174; MYRISTYL 70-75; MYRISTYL 69-74; PKC_PHOSPHO_SITE 101-103; ASN_GLYCOSYLATION 57-60; CK2_PHOSPHO_SITE 214-217; CK2_PHOSPHO_SITE 90-93; MYRISTYL 164-169; MYRISTYL 24-29; CK2_PHOSPHO_SITE 80-83; MYRISTYL 165-170;	Kunitz_BPTI 38-88; KU 131-184; BPTI_KUNITZ_2_2 133-183; sp_O43291_SPT2_HUMAN 38-88; BPTI_KUNITZ_1 66-84; sp_O43291_SPT2_HUMAN 133-183; BPTI_KUNITZ_2_1 38-88; BPTI_KUNITZ_1 161-179; Kunitz_BPTI 133-183; BASICPTASE 73-88; BASICPTASE 63-73; KU 36-89; BASICPTASE 35-49;
DEX0455_041.orf.1	N	0 - o1-53;	16-21,1.006; 4-11,1.105;	PKC_PHOSPHO_SITE 21-23; PKC_PHOSPHO_SITE 42-44; PKC_PHOSPHO_SITE 20-22; MYRISTYL 7-12;	

DEX0455_041.aa.1	N	0 - o1-43;	33-38,1.046; 5-20,1.129;	MYRISTYL 28-33; MYRISTYL 6-11; ASN_GLYCOSYLATION 32-35;	
DEX0455_041.orf.2	N	0 - o1-66;	4-17,1.129; 30-35,1.046;	ASN_GLYCOSYLATION 29-32; MYRISTYL 25-30; PKC_PHOSPHO_SITE 55-57;	
DEX0455_041.aa.2	Y	0 - i1-34;	6-18,1.141; 25-31,1.103;		
DEX0455_042.orf.1	N	0 - o1-116;		PKC_PHOSPHO_SITE 3-5; MYRISTYL 10-15; CK2_PHOSPHO_SITE 7-10; ASN_GLYCOSYLATION 75-78; AMIDATION 40-43; PKC_PHOSPHO_SITE 41-43; CK2_PHOSPHO_SITE 81-84; CK2_PHOSPHO_SITE 36-39; ASN_GLYCOSYLATION 34-37; CK2_PHOSPHO_SITE 72-75; TYR_PHOSPHO_SITE 51-59; CK2_PHOSPHO_SITE 93-96; ASN_GLYCOSYLATION 80-83; PKC_PHOSPHO_SITE 29-31; TYR_PHOSPHO_SITE 40-48; CK2_PHOSPHO_SITE 82-85; CK2_PHOSPHO_SITE 17-20; CK2_PHOSPHO_SITE 56-59; CAMP_PHOSPHO_SITE 69-72; CK2_PHOSPHO_SITE 71-74; CK2_PHOSPHO_SITE 112-115; CK2_PHOSPHO_SITE 76-79; CAMP_PHOSPHO_SITE 42-45; TYR_PHOSPHO_SITE 50-57; PKC_PHOSPHO_SITE 44-46; CK2_PHOSPHO_SITE 77-80; TYR_PHOSPHO_SITE 24-31; CAMP_PHOSPHO_SITE 4-7; PKC_PHOSPHO_SITE 113-115; PKC_PHOSPHO_SITE 71-73; TYR_PHOSPHO_SITE 35-41;	
DEX0455_042.aa.1	N	0 - o1-122;		MYRISTYL 8-13; CK2_PHOSPHO_SITE 87-90; PKC_PHOSPHO_SITE 9-11; CK2_PHOSPHO_SITE 99-102; PKC_PHOSPHO_SITE 47-49; AMIDATION 46-49; CK2_PHOSPHO_SITE 23-26; ASN_GLYCOSYLATION 40-43; TYR_PHOSPHO_SITE 30-37; CK2_PHOSPHO_SITE 88-91; MYRISTYL 16-21; PKC_PHOSPHO_SITE 35-37; CAMP_PHOSPHO_SITE 48-51; ASN_GLYCOSYLATION 7-10; PKC_PHOSPHO_SITE 87-89;	

				TYR_PHOSPHO_SITE 41-47; CK2_PHOSPHO_SITE 42-45;	
DEX0455_043.orf.1	Y	0 - o1-86;	64-72,1.133; 76-83,1.14; 27-38,1.086; 4-20,1.192; 41-50,1.137;	MYRISTYL 3-8; ASN_GLYCOSYLATION 60-63; PKC_PHOSPHO_SITE 29-31; MYRISTYL 64-69; MYRISTYL 56-61; MYRISTYL 61-66;	
DEX0455_043.aa.1	N	0 - o1-30;	11-26,1.155;	CK2_PHOSPHO_SITE 24-27;	
DEX0455_043.orf.2	N	0 - o1-125;		CK2_PHOSPHO_SITE 94-97; MYRISTYL 47-52; PKC_PHOSPHO_SITE 84-86; MYRISTYL 8-13; PKC_PHOSPHO_SITE 77-79;	
DEX0455_043.orf.3	N	0 - i1-104;	89-95,1.052; 59-67,1.023; 10-38,1.08;	PKC_PHOSPHO_SITE 42-44; CK2_PHOSPHO_SITE 34-37; MYRISTYL 9-14; PKC_PHOSPHO_SITE 45-47; PKC_PHOSPHO_SITE 3-5; ASN_GLYCOSYLATION 11-14;	
DEX0455_044.aa.1	N	1 - i1-31;tm32-54;o55-61;	14-24,1.177; 29-58,1.199;	MYRISTYL 27-32;	
DEX0455_045.orf.1	N	0 - o1-193;	178-190,1.144; 135-145,1.124; 121-128,1.095; 70-111,1.15; 25-46,1.115; 51-66,1.216;	AMIDATION 65-68; PKC_PHOSPHO_SITE 129-131; MYRISTYL 10-15; PKC_PHOSPHO_SITE 93-95; MYRISTYL 81-86; CAMP_PHOSPHO_SITE 175-178; AMIDATION 173-176; PKC_PHOSPHO_SITE 5-7; CAMP_PHOSPHO_SITE 110-113; MYRISTYL 83-88; CK2_PHOSPHO_SITE 167-170;	
DEX0455_045.aa.1	N	0 - o1-163;	25-46,1.115; 121-128,1.095; 51-66,1.216; 135-144,1.081; 70-111,1.15;	CK2_PHOSPHO_SITE 149-152; AMIDATION 65-68; PKC_PHOSPHO_SITE 5-7; MYRISTYL 10-15; CAMP_PHOSPHO_SITE 146-149; MYRISTYL 81-86; PKC_PHOSPHO_SITE 93-95; CAMP_PHOSPHO_SITE 110-113; MYRISTYL 83-88; PKC_PHOSPHO_SITE 129-131;	
DEX0455_046.orf.1	N	0 - o1-227;		MYRISTYL 115-120; PKC_PHOSPHO_SITE 3-5; MYRISTYL 97-102; MYRISTYL	

				133-138; CAMP_PHOSPHO_SITE 163-166; CK2_PHOSPHO_SITE 3-6; MYRISTYL 3-8;	
DEX0455_046.aa.1	N	0 - o1-198;	4-11,1.144; 51-59,1.107; 160-184,1.151; 15-25,1.11; 93-99,1.11; 73-85,1.118; 32-40,1.076; 146-153,1.088;	MYRISTYL 90-95; MYRISTYL 71-76; CK2_PHOSPHO_SITE 156-159; MYRISTYL 161-166; PKC_PHOSPHO_SITE 63-65; MYRISTYL 153-158; MYRISTYL 149-154; PKC_PHOSPHO_SITE 119-121; MYRISTYL 86-91; MYRISTYL 157-162; MYRISTYL 68-73; CAMP_PHOSPHO_SITE 120-123; MYRISTYL 104-109;	
DEX0455_047.orf.1	N	0 - o1-103;	66-100,1.232; 23-44,1.101; 10-17,1.088;	AMIDATION 14-17; PKC_PHOSPHO_SITE 73-75; CK2_PHOSPHO_SITE 33-36; PKC_PHOSPHO_SITE 59-61; MYRISTYL 96-101;	
DEX0455_047.aa.1	Y	0 - o1-65;	42-48,1.073; 55-62,1.119; 4-30,1.142; 32-40,1.122;	ASN_GLYCOSYLATION 32-35; CK2_PHOSPHO_SITE 23-26; ASN_GLYCOSYLATION 39-42; MYRISTYL 19-24;	
DEX0455_047.orf.2	N	0 - o1-103;	10-17,1.088; 66-100,1.232; 23-44,1.101;	AMIDATION 14-17; CK2_PHOSPHO_SITE 33-36; MYRISTYL 96-101; PKC_PHOSPHO_SITE 73-75; PKC_PHOSPHO_SITE 59-61;	
DEX0455_047.aa.2	N	0 - o1-27;			
DEX0455_048.aa.1	Y	0 - o1-154;	111-117,1.077; 83-97,1.104; 4-60,1.197; 99-107,1.051; 63-78,1.095; 126-151,1.156;	TYR_PHOSPHO_SITE 105-112; MYRISTYL 80-85; PKC_PHOSPHO_SITE 56-58; CK2_PHOSPHO_SITE 37-40; TYR_PHOSPHO_SITE 79-86;	
DEX0455_048.orf.2	N	0 - o1-176;	151-173,1.203; 86-100.1.104:	PKC_PHOSPHO_SITE 169-171; MYRISTYL 83-88; PKC_PHOSPHO_SITE 59-61; TYR PHOSPHO SITE 108-115:	

			114-120,1.077; 129-141,1.156; 102-110,1.051; 66-81,1.095; 4-63,1.197;	CK2_PHOSPHO_SITE 40-43; TYR_PHOSPHO_SITE 82-89; CK2_PHOSPHO_SITE 24-27;	
DEX0455_048.aa.2	N	0 - o1-271;	39-50,1.182; 4-21,1.232; 181-195,1.104; 98-158,1.148; 246-268,1.203; 161-176,1.095; 197-205,1.051; 66-90,1.192; 224-236,1.156; 209-215,1.077; 57-62,1.053;	TYR_PHOSPHO_SITE 203-210; PKC_PHOSPHO_SITE 154-156; PKC_PHOSPHO_SITE 34-36; RGD 26-28; PKC_PHOSPHO_SITE 264-266; ASN_GLYCOSYLATION 95-98; MYRISTYL 38-43; PKC_PHOSPHO_SITE 21-23; CK2_PHOSPHO_SITE 88-91; TYR_PHOSPHO_SITE 177-184; MYRISTYL 178-183; CK2_PHOSPHO_SITE 135-138; PKC_PHOSPHO_SITE 96-98; CK2_PHOSPHO_SITE 119-122;	
DEX0455_049.aa.1	N	1 - o1-219;tm 220-242;i2 43-268;	199-209,1.147; 129-139,1.104; 95-105,1.087; 4-24,1.212; 219-244,1.317; 58-63,1.099; 145-153,1.156; 69-76,1.121; 86-93,1.085; 163-172,1.122; 176-182,1.056;	PKC_PHOSPHO_SITE 243-245; MYRISTYL 66-71; TYR_PHOSPHO_SITE 105-111; MYRISTYL 77-82; PKC_PHOSPHO_SITE 154-156; CK2_PHOSPHO_SITE 88-91; MYRISTYL 217-222; MYRISTYL 9-14; PKC_PHOSPHO_SITE 81-83; ASN_GLYCOSYLATION 152-155; PKC_PHOSPHO_SITE 115-117; ASN_GLYCOSYLATION 28-31; AMIDATION 32-35; MYRISTYL 29-34; PKC_PHOSPHO_SITE 125-127; MYRISTYL 57-62; CK2_PHOSPHO_SITE 81-84; CK2_PHOSPHO_SITE 157-160; PKC_PHOSPHO_SITE 90-92; MYRISTYL 40-45; ASN_GLYCOSYLATION 65-68; PKC_PHOSPHO_SITE 182-184;	THYROGLOBULIN_1 49-77; thyroglobulin_1 20-89; TY 50-93;
DEX0455_049.aa.2	N	1 - o1-293;tm 294-316:i3	237-246,1.122; 52-67,1.194; 169-	MYRISTYL 10-15; ASN_GLYCOSYLATION 139-142; MYRISTYL 291-296; TYR_PHOSPHO_SITE 179-185; MYRISTYL 29-34:	TY 124-167; thyroglobulin_1 94-163; THYROGLOBULIN_1 123-151;

		17-342;	179,1.087; 132-137,1.099; 219-227,1.156; 41-50,1.059; 203-213,1.104; 273-283,1.147; 250-256,1.056; 24-29,1.038; 293-318,1.317; 73-98,1.193; 143-150,1.121; 160-167,1.085;	PKC_PHOSPHO_SITE 164-166; MYRISTYL 151-156; PKC_PHOSPHO_SITE 228-230; ASN_GLYCOSYLATION 25-28; CK2_PHOSPHO_SITE 231-234; MYRISTYL 32-37; MYRISTYL 140-145; CK2_PHOSPHO_SITE 155-158; PKC_PHOSPHO_SITE 317-319; MYRISTYL 103-108; PKC_PHOSPHO_SITE 155-157; PKC_PHOSPHO_SITE 256-258; MYRISTYL 114-119; ASN_GLYCOSYLATION 226-229; PKC_PHOSPHO_SITE 189-191; MYRISTYL 131-136; PKC_PHOSPHO_SITE 199-201; CK2_PHOSPHO_SITE 162-165; ASN_GLYCOSYLATION 102-105; AMIDATION 106-109; MYRISTYL 80-85;	
DEX0455_049.aa.3	Y	0 - o1-240;	45-70,1.193; 4-22,1.166; 132-139,1.085; 191-199,1.156; 24-39,1.194; 104-109,1.099; 115-122,1.121; 175-185,1.104; 209-216,1.122; 141-151,1.087; 220-237,1.155;	MYRISTYL 112-117; PKC_PHOSPHO_SITE 127-129; PKC_PHOSPHO_SITE 136-138; TYR_PHOSPHO_SITE 151-157; MYRISTYL 10-15; AMIDATION 78-81; ASN_GLYCOSYLATION 198-201; MYRISTYL 86-91; CK2_PHOSPHO_SITE 134-137; MYRISTYL 75-80; PKC_PHOSPHO_SITE 171-173; ASN_GLYCOSYLATION 74-77; PKC_PHOSPHO_SITE 200-202; MYRISTYL 123-128; MYRISTYL 52-57; MYRISTYL 103-108; CK2_PHOSPHO_SITE 127-130; CK2_PHOSPHO_SITE 203-206; PKC_PHOSPHO_SITE 161-163; ASN_GLYCOSYLATION 111-114;	thyroglobulin_1 66-135; TY 96-139; THYROGLOBULIN_1 95-123;
DEX0455_049.aa.4	Y	1 - o1-341;tm 342-364;i3 65-390;	191-198,1.121; 251-261,1.104; 4-23,1.166; 217-227,1.087; 321-331,1.147; 298-304,1.056; 341-366.1.317:	PKC_PHOSPHO_SITE 212-214; CK2_PHOSPHO_SITE 203-206; AMIDATION 154-157; PKC_PHOSPHO_SITE 247-249; PKC_PHOSPHO_SITE 365-367; PKC_PHOSPHO_SITE 94-96; MYRISTYL 151-156; PKC_PHOSPHO_SITE 304-306; CK2_PHOSPHO_SITE 48-51; MYRISTYL 10-15; MYRISTYL 188-193; PKC_PHOSPHO_SITE 237-239; ASN_GLYCOSYLATION 150-153; MYRISTYL 179-184; TYR PHOSPHO SITE 227-233:	thyroglobulin_1 142-211; TY 172-215; THYROGLOBULIN_1 171-199;

			208-215,1.085; 267-275,1.156; 180-185,1.099; 285-294,1.122; 92-115,1.194; 121-146,1.193; 71-77,1.09;	PKC_PHOSPHO_SITE 70-72; RGD 66-68; ASN_GLYCOSYLATION 274-277; PKC_PHOSPHO_SITE 203-205; MYRISTYL 39-44; AMIDATION 81-84; MYRISTYL 128-133; PKC_PHOSPHO_SITE 276-278; MYRISTYL 162-167; ASN_GLYCOSYLATION 187-190; MYRISTYL 199-204; CK2_PHOSPHO_SITE 210-213; MYRISTYL 339-344; CK2_PHOSPHO_SITE 279-282;	
DEX0455_049.aa.5	Y	1 - o1-265;tm266-288;i289-314;	4-22,1.166; 115-122,1.133; 132-139,1.085; 222-228,1.056; 191-199,1.156; 245-255,1.147; 141-151,1.087; 45-70,1.193; 209-218,1.122; 175-185,1.104; 24-39,1.194; 104-109,1.099; 265-290,1.317;	MYRISTYL 86-91; ASN_GLYCOSYLATION 198-201; PKC_PHOSPHO_SITE 127-129; PKC_PHOSPHO_SITE 228-230; MYRISTYL 75-80; MYRISTYL 52-57; MYRISTYL 103-108; CK2_PHOSPHO_SITE 127-130; PKC_PHOSPHO_SITE 289-291; PKC_PHOSPHO_SITE 200-202; TYR_PHOSPHO_SITE 151-157; MYRISTYL 123-128; CK2_PHOSPHO_SITE 203-206; PKC_PHOSPHO_SITE 136-138; ASN_GLYCOSYLATION 111-114; MYRISTYL 263-268; AMIDATION 78-81; CK2_PHOSPHO_SITE 134-137; ASN_GLYCOSYLATION 74-77; PKC_PHOSPHO_SITE 161-163; PKC_PHOSPHO_SITE 171-173; MYRISTYL 10-15; MYRISTYL 112-117;	thyroglobulin_1 66-135; TY 96-139; THYROGLOBULIN_1 95-123;
DEX0455_050.orf.1	Y	1 - i1-11;tm12-31;o32-122;	60-71,1.212; 79-93,1.103; 97-119,1.218; 37-45,1.137; 12-34,1.192;	CK2_PHOSPHO_SITE 72-75; PKC_PHOSPHO_SITE 39-41; PKC_PHOSPHO_SITE 113-115; ASN_GLYCOSYLATION 2-5; CK2_PHOSPHO_SITE 4-7;	PHE_RICH 18-29;
DEX0455_050.aa.1	Y	0 - o1-48;	9-25,1.107; 40-45,1.135;	PKC_PHOSPHO_SITE 4-6; CK2_PHOSPHO_SITE 31-34; MYRISTYL 16-21;	ACTINS_2 29-37;
DEX0455_051.aa.1	N	0 - o1-596;	130-149,1.131; 509-519.1.077:	TYR_PHOSPHO_SITE 182-189; PKC_PHOSPHO_SITE 463-465; PKC_PHOSPHO_SITE 167-169; MYRISTYL 459-464: MYRISTYL	PRO_RICH 407-449; SH3 351-410; SH3DOMAIN 368-383: SH3

			40-45,1.041; 523-540,1.153; 215-230,1.13; 99-105,1.045; 397-422,1.135; 239-258,1.127; 573-579,1.113; 327-334,1.141; 369-383,1.122; 428-443,1.091; 470-477,1.104; 58-76,1.133; 490-496,1.055; 554-568,1.178; 500-506,1.046; 545-551,1.071; 120-128,1.127; 354-361,1.134; 174-182,1.075; 298-304,1.052; 154-160,1.084; 189-205,1.127; 25-31,1.047;	530-535; CK2_PHOSPHO_SITE 46-49; CAMP_PHOSPHO_SITE 65-68; CK2_PHOSPHO_SITE 295-298; CK2_PHOSPHO_SITE 106-109; PKC_PHOSPHO_SITE 241-243; MYRISTYL 524-529; PKC_PHOSPHO_SITE 371-373; MYRISTYL 506-511; CK2_PHOSPHO_SITE 549-552; CK2_PHOSPHO_SITE 12-15; CK2_PHOSPHO_SITE 463-466; CK2_PHOSPHO_SITE 13-16; ASN_GLYCOSYLATION 2-5; CK2_PHOSPHO_SITE 185-188; MYRISTYL 26-31; PKC_PHOSPHO_SITE 384-386; CK2_PHOSPHO_SITE 574-577; CK2_PHOSPHO_SITE 282-285; PKC_PHOSPHO_SITE 260-262; PKC_PHOSPHO_SITE 178-180; CK2_PHOSPHO_SITE 74-77; ASN_GLYCOSYLATION 231-234; MYRISTYL 79-84; PKC_PHOSPHO_SITE 68-70; CK2_PHOSPHO_SITE 260-263; PKC_PHOSPHO_SITE 33-35; ASN_GLYCOSYLATION 366-369; CK2_PHOSPHO_SITE 214-217; MYRISTYL 103-108; CK2_PHOSPHO_SITE 565-568; AMIDATION 163-166; CK2_PHOSPHO_SITE 269-272;	354-409; sp_Q9GZQ2_Q9GZQ2_HUMAN 360-403; SH3DOMAIN 354-364; SH3DOMAIN 396-408; SH3 354-408;
DEX0455_051.aa.2	N	0 - o1-408;	4-41,1.232; 67-83,1.127; 205-212,1.141; 306-321,1.091; 117-136,1.127; 232-239,1.134; 368-	PKC_PHOSPHO_SITE 401-403; CK2_PHOSPHO_SITE 341-344; CK2_PHOSPHO_SITE 63-66; ASN_GLYCOSYLATION 109-112; PKC_PHOSPHO_SITE 56-58; PKC_PHOSPHO_SITE 138-140; PKC_PHOSPHO_SITE 249-251; AMIDATION 401-404; PKC_PHOSPHO_SITE 119-121; PKC_PHOSPHO_SITE 262-264; CK2_PHOSPHO_SITE 138-141; ASN_GLYCOSYLATION 244-247; CK2_PHOSPHO_SITE 147-150;	SH3DOMAIN 274-286; SH3DOMAIN 246-261; SH3 232-286; PRICHEXTENSN 165-182; PRICHEXTENSN 50-62; PRO_RICH 285-327; sp_Q9GZQ2_Q9GZQ2_HUMAN 238-281; SH3 229-288; SH3 232-

			374,1.055; 93-108,1.13; 275-300,1.135; 176-182,1.052; 348-355,1.104; 387-397,1.077; 247-261,1.122; 45-60,1.079; 378-384,1.046;	MYRISTYL 384-389; CK2_PHOSPHO_SITE 92-95; PKC_PHOSPHO_SITE 341-343; MYRISTYL 337-342; TYR_PHOSPHO_SITE 60-67; CK2_PHOSPHO_SITE 160-163; CK2_PHOSPHO_SITE 173-176;	287; SH3DOMAIN 232-242; PRICHEXTENSN 308-320;
DEX0455_051.aa.3	N	0 - o1-470;	383-393,1.077; 428-442,1.178; 344-351,1.104; 374-380,1.046; 4-37,1.232; 41-56,1.079; 271-296,1.135; 447-453,1.113; 419-425,1.071; 243-257,1.122; 113-132,1.127; 228-235,1.134; 302-317,1.091; 172-178,1.052; 201-208,1.141; 89-104,1.13; 63-79,1.127; 397-414,1.153; 364-370,1.055;	CK2_PHOSPHO_SITE 88-91; CK2_PHOSPHO_SITE 423-426; PKC_PHOSPHO_SITE 258-260; CK2_PHOSPHO_SITE 156-159; CK2_PHOSPHO_SITE 169-172; CK2_PHOSPHO_SITE 59-62; CK2_PHOSPHO_SITE 143-146; MYRISTYL 380-385; CK2_PHOSPHO_SITE 134-137; CK2_PHOSPHO_SITE 448-451; ASN_GLYCOSYLATION 105-108; PKC_PHOSPHO_SITE 134-136; PKC_PHOSPHO_SITE 52-54; CK2_PHOSPHO_SITE 439-442; CK2_PHOSPHO_SITE 337-340; PKC_PHOSPHO_SITE 115-117; MYRISTYL 398-403; PKC_PHOSPHO_SITE 337-339; MYRISTYL 404-409; TYR_PHOSPHO_SITE 56-63; ASN_GLYCOSYLATION 240-243; PKC_PHOSPHO_SITE 245-247; MYRISTYL 333-338;	sp_Q9GZQ2_Q9GZQ2_HUMAN 234-277; SH3 228-283; PRICHEXTENSN 304-316; SH3DOMAIN 228-238; PRO_RICH 281-323; SH3 225-284; PRICHEXTENSN 46-58; SH3DOMAIN 270-282; SH3DOMAIN 242-257; SH3 228-282; PRICHEXTENSN 161-178;
DEX0455_051.orf.4	N	0 - o1-474;	378-384,1.046; 45-60.1.079:	PKC_PHOSPHO_SITE 341-343; PKC_PHOSPHO_SITE 262-264; CK2_PHOSPHO_SITE 173-176; PKC PHOSPHO SITE 119-121:	PRO_RICH 285-327; SH3 229-288; PRICHEXTENSN

			306-321,1.091; 176-182,1.052; 67-83,1.127; 232-239,1.134; 247-261,1.122; 93-108,1.13; 432-446,1.178; 117-136,1.127; 451-457,1.113; 205-212,1.141; 4-41,1.232; 348-355,1.104; 275-300,1.135; 387-397,1.077; 368-374,1.055; 423-429,1.071; 401-418,1.153;	CK2_PHOSPHO_SITE 63-66; CK2_PHOSPHO_SITE 138-141; CK2_PHOSPHO_SITE 160-163; CK2_PHOSPHO_SITE 452-455; MYRISTYL 384-389; PKC_PHOSPHO_SITE 138-140; ASN_GLYCOSYLATION 109-112; CK2_PHOSPHO_SITE 427-430; TYR_PHOSPHO_SITE 60-67; PKC_PHOSPHO_SITE 249-251; CK2_PHOSPHO_SITE 341-344; MYRISTYL 402-407; CK2_PHOSPHO_SITE 147-150; MYRISTYL 408-413; CK2_PHOSPHO_SITE 443-446; PKC_PHOSPHO_SITE 56-58; MYRISTYL 337-342; CK2_PHOSPHO_SITE 92-95; ASN_GLYCOSYLATION 244-247;	165-182; SH3DOMAIN 274-286; SH3DOMAIN 246-261; SH3DOMAIN 232-242; PRICHEXTENSN 308-320; PRICHEXTENSN 50-62; sp_Q9GZQ2_Q9GZQ2_HUMAN 238-281; SH3 232-287; SH3 232-286;
DEX0455_051.orf.5	N	0 - o1-474;	306-321,1.091; 93-108,1.13; 232-239,1.134; 423-429,1.071; 451-457,1.113; 247-261,1.122; 432-446,1.178; 348-355,1.104; 401-418,1.153; 368-374,1.055; 45-60,1.079; 275-300,1.135; 387-	ASN_GLYCOSYLATION 244-247; PKC_PHOSPHO_SITE 249-251; CK2_PHOSPHO_SITE 341-344; CK2_PHOSPHO_SITE 443-446; MYRISTYL 402-407; PKC_PHOSPHO_SITE 119-121; PKC_PHOSPHO_SITE 56-58; CK2_PHOSPHO_SITE 160-163; PKC_PHOSPHO_SITE 138-140; CK2_PHOSPHO_SITE 63-66; MYRISTYL 337-342; TYR_PHOSPHO_SITE 60-67; CK2_PHOSPHO_SITE 92-95; CK2_PHOSPHO_SITE 173-176; MYRISTYL 408-413; ASN_GLYCOSYLATION 109-112; MYRISTYL 384-389; CK2_PHOSPHO_SITE 427-430; CK2_PHOSPHO_SITE 452-455; CK2_PHOSPHO_SITE 138-141; PKC_PHOSPHO_SITE 341-343; CK2_PHOSPHO_SITE 147-150; PKC_PHOSPHO_SITE 262-264;	PRO_RICH 285-327; SH3 232-287; PRICHEXTENSN 308-320; SH3DOMAIN 246-261; SH3DOMAIN 232-242; PRICHEXTENSN 165-182; SH3 232-286; PRICHEXTENSN 50-62; sp_Q9GZQ2_Q9GZQ2_HUMAN 238-281; SH3DOMAIN 274-286; SH3 229-288;

			397,1.077; 205-212,1.141; 176-182,1.052; 378-384,1.046; 117-136,1.127; 67-83,1.127; 4-41,1.232;		
DEX0455_051.orf.6	N	0 - o1-474;	368-374,1.055; 205-212,1.141; 348-355,1.104; 93-108,1.13; 275-300,1.135; 45-60,1.079; 176-182,1.052; 401-418,1.153; 378-384,1.046; 67-83,1.127; 117-136,1.127; 387-397,1.077; 4-41,1.232; 232-239,1.134; 306-321,1.091; 423-429,1.071; 432-446,1.178; 451-457,1.113; 247-261,1.122;	CK2_PHOSPHO_SITE 443-446; CK2_PHOSPHO_SITE 452-455; PKC_PHOSPHO_SITE 56-58; MYRISTYL 408-413; CK2_PHOSPHO_SITE 63-66; MYRISTYL 402-407; CK2_PHOSPHO_SITE 147-150; MYRISTYL 384-389; TYR_PHOSPHO_SITE 60-67; ASN_GLYCOSYLATION 109-112; MYRISTYL 337-342; CK2_PHOSPHO_SITE 138-141; CK2_PHOSPHO_SITE 92-95; PKC_PHOSPHO_SITE 119-121; CK2_PHOSPHO_SITE 173-176; ASN_GLYCOSYLATION 244-247; PKC_PHOSPHO_SITE 249-251; CK2_PHOSPHO_SITE 160-163; PKC_PHOSPHO_SITE 138-140; PKC_PHOSPHO_SITE 341-343; PKC_PHOSPHO_SITE 262-264; CK2_PHOSPHO_SITE 341-344; CK2_PHOSPHO_SITE 427-430;	SH3 229-288; SH3DOMAIN 232-242; SH3DOMAIN 246-261; PRICHEXTENSN 308-320; sp_Q9GZQ2_Q9GZQ2_HUMAN 238-281; PRICHEXTENSN 50-62; PRICHEXTENSN 165-182; SH3 232-286; SH3DOMAIN 274-286; PRO_RICH 285-327; SH3 232-287;
DEX0455_052.aa.1	N	0 - o1-470;	63-79,1.127; 271-296,1.135; 383-393,1.077; 243-257,1.122;	PKC_PHOSPHO_SITE 258-260; CK2_PHOSPHO_SITE 423-426; CK2_PHOSPHO_SITE 59-62; PKC_PHOSPHO_SITE 245-247; PKC_PHOSPHO_SITE 52-54; CK2_PHOSPHO_SITE 143-146; CK2_PHOSPHO_SITE 134-137; CK2_PHOSPHO_SITE 88-91;	PRO_RICH 281-323; PRICHEXTENSN 161-178; SH3 228-283; PRICHEXTENSN 304-316; SH3DOMAIN 270-

			4-37,1.232; 89-104,1.13; 374-380,1.046; 41-56,1.079; 397-414,1.153; 364-370,1.055; 419-425,1.071; 302-317,1.091; 172-178,1.052; 447-453,1.113; 228-235,1.134; 344-351,1.104; 201-208,1.141; 113-132,1.127; 428-442,1.178;	PKC_PHOSPHO_SITE 134-136; ASN_GLYCOSYLATION 105-108; PKC_PHOSPHO_SITE 337-339; MYRISTYL 398-403; ASN_GLYCOSYLATION 240-243; TYR_PHOSPHO_SITE 56-63; MYRISTYL 333-338; CK2_PHOSPHO_SITE 439-442; MYRISTYL 380-385; PKC_PHOSPHO_SITE 115-117; CK2_PHOSPHO_SITE 337-340; CK2_PHOSPHO_SITE 448-451; MYRISTYL 404-409; CK2_PHOSPHO_SITE 169-172; CK2_PHOSPHO_SITE 156-159;	282; SH3DOMAIN 242-257; SH3 228-282; SH3DOMAIN 228-238; PRICHEXTENSN 46-58; SH3 225-284; sp_Q9GZQ2_Q9GZQ2_HUMAN 234-277;
DEX0455_052.aa.2	N	0 - o1-502;	479-485,1.113; 260-267,1.134; 223-240,1.141; 406-412,1.046; 303-328,1.135; 376-383,1.104; 451-457,1.071; 415-425,1.077; 275-289,1.122; 4-37,1.232; 334-349,1.091; 63-79,1.127; 113-132,1.127; 396-402,1.055; 172-	CK2_PHOSPHO_SITE 156-159; CK2_PHOSPHO_SITE 455-458; CK2_PHOSPHO_SITE 59-62; CK2_PHOSPHO_SITE 134-137; PKC_PHOSPHO_SITE 290-292; CK2_PHOSPHO_SITE 369-372; MYRISTYL 365-370; ASN_GLYCOSYLATION 105-108; ASN_GLYCOSYLATION 272-275; TYR_PHOSPHO_SITE 56-63; PKC_PHOSPHO_SITE 277-279; CK2_PHOSPHO_SITE 88-91; PKC_PHOSPHO_SITE 52-54; CK2_PHOSPHO_SITE 143-146; PKC_PHOSPHO_SITE 115-117; MYRISTYL 412-417; MYRISTYL 430-435; PKC_PHOSPHO_SITE 134-136; CK2_PHOSPHO_SITE 169-172; MYRISTYL 436-441; CK2_PHOSPHO_SITE 471-474; CK2_PHOSPHO_SITE 480-483; PKC_PHOSPHO_SITE 369-371;	SH3DOMAIN 302-314; sp_Q9GZQ2_Q9GZQ2_HUMAN 266-309; SH3DOMAIN 274-289; SH3 257-316; SH3 260-314; SH3 260-315; SH3DOMAIN 260-270; PRO_RICH 313-355;

			178,1.052; 429-446,1.153; 89-104,1.13; 460-474,1.178; 41-56,1.079;		
DEX0455_052.aa.3	Y	0 - o1-548;	4-29,1.211; 79-95,1.162; 56-73,1.118; 495-502,1.134; 510-519,1.1; 167-185,1.133; 239-258,1.131; 263-269,1.084; 99-109,1.259; 208-214,1.045; 407-413,1.052; 298-314,1.127; 134-140,1.047; 324-339,1.13; 42-48,1.082; 149-154,1.041; 348-367,1.127; 525-531,1.113; 283-291,1.075; 113-127,1.116; 458-475,1.141; 229-237,1.127;	PKC_PHOSPHO_SITE 512-514; MYRISTYL 135-140; ASN_GLYCOSYLATION 340-343; MYRISTYL 188-193; PKC_PHOSPHO_SITE 41-43; CK2_PHOSPHO_SITE 36-39; CK2_PHOSPHO_SITE 391-394; PKC_PHOSPHO_SITE 350-352; AMIDATION 1-4; CK2_PHOSPHO_SITE 294-297; PKC_PHOSPHO_SITE 276-278; MYRISTYL 212-217; CK2_PHOSPHO_SITE 183-186; PKC_PHOSPHO_SITE 287-289; ASN_GLYCOSYLATION 12-15; PKC_PHOSPHO_SITE 369-371; CK2_PHOSPHO_SITE 74-77; CK2_PHOSPHO_SITE 323-326; CK2_PHOSPHO_SITE 369-372; CAMP_PHOSPHO_SITE 174-177; CK2_PHOSPHO_SITE 68-71; TYR_PHOSPHO_SITE 291-298; AMIDATION 272-275; CK2_PHOSPHO_SITE 404-407; PKC_PHOSPHO_SITE 177-179; CK2_PHOSPHO_SITE 155-158; CK2_PHOSPHO_SITE 215-218; ASN_GLYCOSYLATION 507-510; CK2_PHOSPHO_SITE 526-529; CK2_PHOSPHO_SITE 378-381; PKC_PHOSPHO_SITE 142-144; MYRISTYL 121-126;	
DEX0455_052.aa.4	Y	0 - o1-277;	78-103,1.135; 109-124,1.091; 235-249,1.178;	MYRISTYL 2-7; PKC_PHOSPHO_SITE 16-18; CK2_PHOSPHO_SITE 230-233; MYRISTYL 211-216; CK2_PHOSPHO_SITE 246-249; MYRISTYL 205-210;	SH3DOMAIN 77-89; PRICHEXTENSN 170-195; PRICHEXTENSN 112-128; SH3

			254-260,1.113; 4-19,1.169; 151-158,1.104; 181-187,1.046; 204-221,1.153; 190-200,1.077; 50-64,1.122; 226-232,1.071; 35-42,1.134; 171-177,1.055;	CK2_PHOSPHO_SITE 255-258; CK2_PHOSPHO_SITE 144-147; PKC_PHOSPHO_SITE 65-67; MYRISTYL 140-145; PKC_PHOSPHO_SITE 144-146; ASN_GLYCOSYLATION 47-50; CK2_PHOSPHO_SITE 16-19; PKC_PHOSPHO_SITE 52-54; MYRISTYL 187-192;	35-89; PRICHEXTENSN 88-109; PRO_RICH 88-130; SH3 32-91; SH3DOMAIN 35-45; SH3 35-90; sp_Q9GZQ2_Q9GZQ2_HUMAN 41-84; SH3DOMAIN 49-64;
DEX0455_053.aa.1	Y	1 - i1-6;tm7-29;o30-282;	73-83,1.16; 36-45,1.103; 152-160,1.069; 176-186,1.162; 127-134,1.125; 207-217,1.215; 53-59,1.066; 61-71,1.119; 248-279,1.179; 100-123,1.136; 165-171,1.06; 4-30,1.146;	ASN_GLYCOSYLATION 112-115; CK2_PHOSPHO_SITE 91-94; ASN_GLYCOSYLATION 216-219; CK2_PHOSPHO_SITE 151-154; CAMP_PHOSPHO_SITE 246-249; ASN_GLYCOSYLATION 196-199; PKC_PHOSPHO_SITE 32-34; MYRISTYL 188-193; CK2_PHOSPHO_SITE 183-186; PKC_PHOSPHO_SITE 207-209; ASN_GLYCOSYLATION 190-193; ASN_GLYCOSYLATION 160-163; MYRISTYL 52-57; PKC_PHOSPHO_SITE 127-129; ASN_GLYCOSYLATION 205-208; CK2_PHOSPHO_SITE 241-244; PKC_PHOSPHO_SITE 134-136; CK2_PHOSPHO_SITE 197-200; PKC_PHOSPHO_SITE 165-167; PKC_PHOSPHO_SITE 114-116; ASN_GLYCOSYLATION 220-223; MYRISTYL 126-131;	IG_LIKE_2 153-241; IG_LIKE_1 49-151;
DEX0455_053.aa.2	Y	1 - i1-6;tm7-29;o30-59;	4-39,1.146; 41-56,1.17;		
DEX0455_053.aa.3	N	0 - o1-252;	177-187,1.215; 43-53,1.16; 23-29,1.1; 122-130,1.069; 146-156,1.162; 218-	ASN_GLYCOSYLATION 166-169; PKC_PHOSPHO_SITE 177-179; PKC_PHOSPHO_SITE 97-99; CK2_PHOSPHO_SITE 153-156; PKC_PHOSPHO_SITE 104-106; ASN_GLYCOSYLATION 160-163; CK2_PHOSPHO_SITE 167-170; ASN_GLYCOSYLATION 186-189; CAMP_PHOSPHO_SITE 216-219; CK2_PHOSPHO_SITE 61-64;	IG_LIKE_1 19-121; ig 19-102; IG 11-116; IG_LIKE_2 123-211;

			249,1.179; 6-15,1.103; 70-93,1.136; 97-104,1.125; 135-141,1.06; 31-41,1.119;	ASN_GLYCOSYLATION 82-85; CK2_PHOSPHO_SITE 121-124; PKC_PHOSPHO_SITE 84-86; CK2_PHOSPHO_SITE 211-214; ASN_GLYCOSYLATION 190-193; MYRISTYL 158-163; ASN_GLYCOSYLATION 130-133; MYRISTYL 96-101; MYRISTYL 22-27; PKC_PHOSPHO_SITE 135-137; ASN_GLYCOSYLATION 175-178;	
DEX0455_054.orf.1	N	0 - o1-155;	6-13,1.134; 145-152,1.23; 34-51,1.251; 53-87,1.163; 21-30,1.088; 99-123,1.205;	CK2_PHOSPHO_SITE 72-75; PKC_PHOSPHO_SITE 67-69; AMIDATION 124-127; MYRISTYL 109-114; MYRISTYL 79-84; CK2_PHOSPHO_SITE 89-92;	PRO_RICH 51-70;
DEX0455_054.aa.1	N	0 - o1-107;	23-31,1.113; 4-20,1.19; 61-67,1.089; 36-57,1.184; 81-90,1.191;	PKC_PHOSPHO_SITE 100-102; MYRISTYL 94-99; PKC_PHOSPHO_SITE 35-37;	sp_P14786_KPY2_HUMAN 12-105; PK_C 3-105;
DEX0455_054.orf.2	N	0 - o1-155;	99-123,1.205; 6-13,1.134; 53-87,1.163; 145-152,1.23; 34-51,1.251; 21-30,1.088;	AMIDATION 124-127; CK2_PHOSPHO_SITE 89-92; MYRISTYL 79-84; PKC_PHOSPHO_SITE 67-69; MYRISTYL 109-114; CK2_PHOSPHO_SITE 72-75;	PRO_RICH 51-70;
DEX0455_054.aa.2	N	0 - o1-143;	28-45,1.179; 72-93,1.184; 50-56,1.095; 117-126,1.191; 7-14,1.1; 97-103,1.089; 59-67,1.113;	MYRISTYL 27-32; PKC_PHOSPHO_SITE 32-34; PKC_PHOSPHO_SITE 136-138; PKC_PHOSPHO_SITE 71-73; MYRISTYL 130-135; PKC_PHOSPHO_SITE 46-48;	PK_C 21-141; sp_P11974_KPY1_RABIT 1-141;
DEX0455	N	0 -		MYRISTYL 52-57;	

_055.aa .1		o1- 253;		CK2_PHOSPHO_SITE 11-14; PKC_PHOSPHO_SITE 19-21; PKC_PHOSPHO_SITE 207-209; CK2_PHOSPHO_SITE 9-12; PKC_PHOSPHO_SITE 164-166; CK2_PHOSPHO_SITE 7-10; CAMP_PHOSPHO_SITE 131-134; PKC_PHOSPHO_SITE 130-132; PKC_PHOSPHO_SITE 245-247; CK2_PHOSPHO_SITE 243-246; AMIDATION 176-179; CK2_PHOSPHO_SITE 19-22;	
DEX0455 _055.aa .2	N	0 - o1- 361;	107- 114,1.114; 42- 52,1.147; 83- 97,1.14; 70- 76,1.055; 236- 242,1.115; 4- 11,1.148; 320- 326,1.056; 164- 186,1.208; 124- 135,1.132; 273- 278,1.03; 99- 105,1.047; 224- 230,1.064;	CAMP_PHOSPHO_SITE 18-21; CK2_PHOSPHO_SITE 12-15; AMIDATION 348-351; MYRISTYL 107-112; PKC_PHOSPHO_SITE 344-346; CAMP_PHOSPHO_SITE 186-189; MYRISTYL 311-316; CAMP_PHOSPHO_SITE 309-312; PKC_PHOSPHO_SITE 325-327; AMIDATION 231-234; CK2_PHOSPHO_SITE 62-65; MYRISTYL 22-27; CK2_PHOSPHO_SITE 66-69; ASN_GLYCOSYLATION 358-361; PKC_PHOSPHO_SITE 262-264; AMIDATION 306-309; PKC_PHOSPHO_SITE 16-18; CK2_PHOSPHO_SITE 74-77; PKC_PHOSPHO_SITE 185-187; PKC_PHOSPHO_SITE 219-221; PKC_PHOSPHO_SITE 74-76; CK2_PHOSPHO_SITE 319-322; AMIDATION 339-342; CK2_PHOSPHO_SITE 64-67; CAMP_PHOSPHO_SITE 341-344; PKC_PHOSPHO_SITE 293-295;	
DEX0455 _055.aa .3	N	0 - i1- 167;	28- 49,1.115; 126- 137,1.056; 68- 84,1.038; 4- 10,1.009; 12- 19,1.035; 60- 66,1.026;	AMIDATION 112-115; MYRISTYL 117-122; PKC_PHOSPHO_SITE 25-27; PKC_PHOSPHO_SITE 131-133; PKC_PHOSPHO_SITE 150-152; AMIDATION 145-148; CAMP_PHOSPHO_SITE 147-150; CK2_PHOSPHO_SITE 125-128; PKC_PHOSPHO_SITE 99-101; AMIDATION 37-40; CAMP_PHOSPHO_SITE 115-118; AMIDATION 154-157; PKC_PHOSPHO_SITE 68-70; ASN_GLYCOSYLATION 164-167;	
DEX0455 _056.or f.1	N	0 - o1- 636;	53- 59,1.147; 401- 411,1.092; 4- 10,1.067; 592-	ASN_GLYCOSYLATION 199-202; MYRISTYL 65-70; MYRISTYL 451-456; CK2_PHOSPHO_SITE 221-224; ASN_GLYCOSYLATION 454-457; CK2_PHOSPHO_SITE 574-577; CK2_PHOSPHO_SITE 115-118; MYRISTYL 531-536;	

			633,1.179; 218-253,1.106; 474-480,1.058; 95-136,1.207; 440-448,1.082; 354-372,1.185; 165-203,1.177; 66-74,1.083; 429-437,1.111; 142-148,1.091; 153-163,1.075; 274-285,1.132; 374-386,1.187; 578-584,1.107; 530-574,1.129; 460-466,1.147; 76-83,1.118; 490-518,1.111; 259-265,1.052; 290-302,1.163; 309-325,1.128;	CK2_PHOSPHO_SITE 347-350; CK2_PHOSPHO_SITE 137-140; CK2_PHOSPHO_SITE 308-311; CK2_PHOSPHO_SITE 301-304; MYRISTYL 336-341; MYRISTYL 154-159; PKC_PHOSPHO_SITE 201-203; MYRISTYL 231-236; CK2_PHOSPHO_SITE 525-528; ASN_GLYCOSYLATION 415-418; MYRISTYL 206-211; PKC_PHOSPHO_SITE 565-567; PKC_PHOSPHO_SITE 286-288; TYR_PHOSPHO_SITE 351-357; MYRISTYL 60-65; TYR_PHOSPHO_SITE 421-428; AMIDATION 20-23; CK2_PHOSPHO_SITE 70-73; MYRISTYL 63-68; PKC_PHOSPHO_SITE 70-72; CK2_PHOSPHO_SITE 293-296; MYRISTYL 588-593; MYRISTYL 51-56; CAMP_PHOSPHO_SITE 23-26; ASN_GLYCOSYLATION 548-551; CK2_PHOSPHO_SITE 35-38; MYRISTYL 4-9; MYRISTYL 11-16; CK2_PHOSPHO_SITE 235-238; CK2_PHOSPHO_SITE 286-289; MYRISTYL 49-54;	
DEX0455_056.aa.1	N	0 - o1-870;	38-44,1.147; 386-396,1.092; 690-699,1.137; 679-688,1.065; 339-357,1.185; 259-270,1.132; 634-652,1.134; 515-559,1.129; 51-59.1.083:	CK2_PHOSPHO_SITE 559-562; CK2_PHOSPHO_SITE 122-125; MYRISTYL 659-664; MYRISTYL 36-41; MYRISTYL 34-39; PKC_PHOSPHO_SITE 271-273; CK2_PHOSPHO_SITE 510-513; MYRISTYL 45-50; TYR_PHOSPHO_SITE 406-413; CK2_PHOSPHO_SITE 206-209; MYRISTYL 834-839; PKC_PHOSPHO_SITE 664-666; CK2_PHOSPHO_SITE 332-335; ASN_GLYCOSYLATION 533-536; MYRISTYL 436-441; MYRISTYL 139-144; MYRISTYL 191-196; MYRISTYL 573-578; PKC_PHOSPHO_SITE 550-552; CK2 PHOSPHO SITE 220-223:	

			425-433,1.082; 294-310,1.128; 445-451,1.147; 275-287,1.163; 244-250,1.052; 763-796,1.144; 459-465,1.058; 827-844,1.127; 150-188,1.177; 414-422,1.111; 739-754,1.163; 659-664,1.038; 707-723,1.101; 359-371,1.187; 798-805,1.037; 203-238,1.106; 80-121,1.207; 563-569,1.107; 851-867,1.148; 577-629,1.179; 475-503,1.111; 127-133,1.091; 138-148,1.075; 61-68,1.118; 666-676,1.164;	PKC_PHOSPHO_SITE 762-764; CK2_PHOSPHO_SITE 100-103; CK2_PHOSPHO_SITE 824-827; CK2_PHOSPHO_SITE 640-643; MYRISTYL 321-326; PKC_PHOSPHO_SITE 55-57; PKC_PHOSPHO_SITE 186-188; CK2_PHOSPHO_SITE 20-23; CK2_PHOSPHO_SITE 286-289; MYRISTYL 216-221; CK2_PHOSPHO_SITE 278-281; PKC_PHOSPHO_SITE 842-844; ASN_GLYCOSYLATION 184-187; CAMP_PHOSPHO_SITE 748-751; MYRISTYL 516-521; MYRISTYL 50-55; TYR_PHOSPHO_SITE 336-342; PKC_PHOSPHO_SITE 756-758; ASN_GLYCOSYLATION 439-442; ASN_GLYCOSYLATION 400-403; AMIDATION 5-8; PKC_PHOSPHO_SITE 824-826; CAMP_PHOSPHO_SITE 8-11; CK2_PHOSPHO_SITE 293-296; CK2_PHOSPHO_SITE 55-58; CK2_PHOSPHO_SITE 271-274; MYRISTYL 48-53;	
DEX0455_056.aa.2	N	0 - o1-791;	244-250,1.052; 51-59,1.083; 339-357,1.185; 577-619,1.179; 772-	CAMP_PHOSPHO_SITE 738-741; PKC_PHOSPHO_SITE 55-57; CK2_PHOSPHO_SITE 220-223; CK2_PHOSPHO_SITE 100-103; CK2_PHOSPHO_SITE 122-125; CK2_PHOSPHO_SITE 271-274; CK2_PHOSPHO_SITE 286-289; CAMP_PHOSPHO_SITE 8-11; PKC PHOSPHO SITE 654-656:	

			788,1.148; 669-678,1.065; 138-148,1.075; 656-666,1.164; 294-310,1.128; 475-503,1.111; 515-559,1.129; 459-465,1.058; 697-713,1.101; 386-396,1.092; 624-642,1.134; 445-451,1.147; 127-133,1.091; 680-689,1.137; 38-44,1.147; 359-371,1.187; 259-270,1.132; 414-422,1.111; 563-569,1.107; 753-765,1.127; 203-238,1.106; 425-433,1.082; 729-744,1.163; 275-287,1.163; 150-188,1.177; 80-121,1.207; 61-68,1.118; 649-654,1.038;	MYRISTYL 191-196; MYRISTYL 516-521; CK2_PHOSPHO_SITE 510-513; MYRISTYL 36-41; PKC_PHOSPHO_SITE 763-765; CK2_PHOSPHO_SITE 630-633; MYRISTYL 321-326; CK2_PHOSPHO_SITE 332-335; PKC_PHOSPHO_SITE 271-273; MYRISTYL 216-221; PKC_PHOSPHO_SITE 186-188; CK2_PHOSPHO_SITE 293-296; MYRISTYL 139-144; ASN_GLYCOSYLATION 439-442; MYRISTYL 573-578; AMIDATION 5-8; MYRISTYL 50-55; PKC_PHOSPHO_SITE 752-754; PKC_PHOSPHO_SITE 550-552; ASN_GLYCOSYLATION 533-536; TYR_PHOSPHO_SITE 406-413; MYRISTYL 48-53; PKC_PHOSPHO_SITE 746-748; CK2_PHOSPHO_SITE 559-562; ASN_GLYCOSYLATION 400-403; MYRISTYL 34-39; MYRISTYL 436-441; CK2_PHOSPHO_SITE 278-281; CK2_PHOSPHO_SITE 206-209; MYRISTYL 649-654; CK2_PHOSPHO_SITE 20-23; ASN_GLYCOSYLATION 184-187; TYR_PHOSPHO_SITE 336-342; MYRISTYL 755-760; CK2_PHOSPHO_SITE 55-58; MYRISTYL 45-50;	
DEX0455_057.orf.1	N	0 - o1-122;	97-119,1.114; 30-41.1.138:	PKC_PHOSPHO_SITE 3-5; ASN_GLYCOSYLATION 48-51; CK2_PHOSPHO_SITE 25-28; PKC PHOSPHO SITE 27-29:	EF_HAND_2 25-101; S100_CABP 80-101; EFh 76-104:

			4-13,1.125;	CK2_PHOSPHO_SITE 23-26; PKC_PHOSPHO_SITE 118-120; MYRISTYL 103-108; CK2_PHOSPHO_SITE 12-15; CK2_PHOSPHO_SITE 86-89; CK2_PHOSPHO_SITE 52-55;	sp_P31949_S111_HUMAN 25-94; S_100 27-70; efhand 76-104; sp_O93395_O93395_SALFO 44-98; EF_HAND 85-97;
DEX0455_057.aa.1	N	0 - o1-170;	78-89,1.138; 145-167,1.114; 4-38,1.16;	ASN_GLYCOSYLATION 96-99; CK2_PHOSPHO_SITE 71-74; PKC_PHOSPHO_SITE 55-57; CK2_PHOSPHO_SITE 43-46; PKC_PHOSPHO_SITE 75-77; CK2_PHOSPHO_SITE 134-137; PKC_PHOSPHO_SITE 166-168; CK2_PHOSPHO_SITE 100-103; MYRISTYL 151-156; CK2_PHOSPHO_SITE 73-76; PKC_PHOSPHO_SITE 58-60; CK2_PHOSPHO_SITE 6-9;	sp_P31949_S111_HUMAN 73-142; EF_HAND 133-145; S100_CABP 128-149; sp_O93395_O93395_SALFO 92-146; efhand 124-152; EFh 124-152; S_100 75-118; EF_HAND_2 73-149;
DEX0455_057.aa.2	N	0 - o1-91;	66-88,1.114; 4-11,1.134;	CK2_PHOSPHO_SITE 55-58; ASN_GLYCOSYLATION 17-20; PKC_PHOSPHO_SITE 87-89; CK2_PHOSPHO_SITE 21-24; MYRISTYL 72-77;	EFh 45-73; efhand 45-73; S100_CABP 49-70; S_100 3-39; EF_HAND 54-66; sp_P31949_S111_HUMAN 9-63; EF_HAND_2 19-70; sp_O93395_O93395_SALFO 13-67;
DEX0455_058.orf.1	N	1 - o1-14;tm15-37;i38-66;	4-25,1.178; 27-63,1.191;	CK2_PHOSPHO_SITE 23-26; MYRISTYL 27-32;	
DEX0455_058.aa.1	N	0 - o1-65;	24-32,1.155; 36-54,1.162; 14-22,1.084;	TYR_PHOSPHO_SITE 12-18; ASN_GLYCOSYLATION 59-62; CK2_PHOSPHO_SITE 6-9;	
DEX0455_059.orf.1	N	0 - o1-363;	104-122,1.145; 261-268,1.085; 11-21,1.113; 341-351,1.191; 125-159,1.118; 178-212,1.171; 69-77,1.128; 315-330.1.192;	PKC_PHOSPHO_SITE 80-82; CK2_PHOSPHO_SITE 28-31; PKC_PHOSPHO_SITE 281-283; CAMP_PHOSPHO_SITE 105-108; MYRISTYL 47-52; CAMP_PHOSPHO_SITE 77-80; PKC_PHOSPHO_SITE 103-105; MYRISTYL 335-340; PKC_PHOSPHO_SITE 206-208; PKC_PHOSPHO_SITE 76-78; MYRISTYL 304-309; MYRISTYL 71-76; PKC_PHOSPHO_SITE 28-30; PKC_PHOSPHO_SITE 8-10; CK2_PHOSPHO_SITE 17-20; PKC_PHOSPHO_SITE 62-64; CK2_PHOSPHO_SITE 237-	

			270-275,1.039; 235-248,1.131; 281-289,1.116; 353-360,1.134; 85-102,1.157; 295-305,1.07; 225-232,1.131;	240;	
DEX0455_059.aa.1	N	0 - o1-116;	38-67,1.204; 28-34,1.111; 12-23,1.084; 71-113,1.168;	PKC_PHOSPHO_SITE 25-27; PKC_PHOSPHO_SITE 58-60; AMIDATION 16-19; CK2_PHOSPHO_SITE 5-8; PKC_PHOSPHO_SITE 45-47;	
DEX0455_059.orf.2	N	0 - o1-166;	118-133,1.192; 16-26,1.124; 98-108,1.07; 144-154,1.191; 64-71,1.085; 7-13,1.026; 38-51,1.131; 84-92,1.116; 28-35,1.122; 156-163,1.134; 73-78,1.039;	MYRISTYL 107-112; CK2_PHOSPHO_SITE 40-43; MYRISTYL 138-143; PKC_PHOSPHO_SITE 84-86;	
DEX0455_060.aa.1	Y	0 - o1-207;	115-122,1.108; 149-187,1.215; 193-199,1.122; 4-26,1.251; 138-145,1.131; 43-56,1.102; 87-101,1.175;	MYRISTYL 76-81; AMIDATION 79-82; PKC_PHOSPHO_SITE 42-44; MYRISTYL 34-39; MYRISTYL 41-46; PKC_PHOSPHO_SITE 24-26; MYRISTYL 75-80;	BTG_1 124-144; ANTIPRLFBTG1 173-202; Anti_proliferat 83-207; BTG_2 170-189; btg1 83-190; ANTIPRLFBTG1 88-112; ANTIPRLFBTG1 113-142;

DEX0455_061.aa.1	N	0 - o1-352;	173-179,1.031; 264-290,1.129; 181-187,1.04; 138-148,1.114; 36-68,1.256; 4-10,1.15; 108-113,1.105; 230-241,1.187; 120-128,1.086; 249-257,1.172; 344-349,1.095; 14-20,1.171; 208-225,1.103; 333-340,1.068; 81-91,1.111; 292-319,1.15;	MYRISTYL 57-62; CK2_PHOSPHO_SITE 22-25; MYRISTYL 133-138; CK2_PHOSPHO_SITE 150-153; PKC_PHOSPHO_SITE 178-180; ASN_GLYCOSYLATION 134-137; MYRISTYL 43-48; AMIDATION 10-13; CAMP_PHOSPHO_SITE 119-122; CK2_PHOSPHO_SITE 314-317; ASN_GLYCOSYLATION 225-228; TYR_PHOSPHO_SITE 263-269; PKC_PHOSPHO_SITE 331-333; CK2_PHOSPHO_SITE 170-173; MYRISTYL 217-222;	RA 203-293; RA_DOMAIN 205-293; RA 203-293;
DEX0455_061.aa.2	N	0 - o1-261;	230-241,1.187; 108-113,1.105; 173-179,1.031; 208-225,1.103; 36-68,1.256; 81-91,1.111; 249-258,1.172; 138-148,1.114; 120-128,1.086; 4-10,1.15; 14-20,1.171; 181-187,1.04;	ASN_GLYCOSYLATION 134-137; MYRISTYL 43-48; CAMP_PHOSPHO_SITE 119-122; MYRISTYL 57-62; CK2_PHOSPHO_SITE 150-153; PKC_PHOSPHO_SITE 178-180; AMIDATION 10-13; CK2_PHOSPHO_SITE 22-25; MYRISTYL 217-222; ASN_GLYCOSYLATION 225-228; MYRISTYL 133-138; CK2_PHOSPHO_SITE 170-173;	RA 203-260; RA_DOMAIN 205-261;
DEX0455_061.aa.3	N	0 - o1-269;	181-187,1.04; 36-68,1.256; 120-	CK2_PHOSPHO_SITE 22-25; CK2_PHOSPHO_SITE 258-261; MYRISTYL 133-138; CK2_PHOSPHO_SITE 170-173; CK2_PHOSPHO_SITE 150-153;	RA 203-269; RA_DOMAIN 205-269;

			128,1.086; 230-241,1.187; 14-20,1.171; 4-10,1.15; 173-179,1.031; 108-113,1.105; 81-91,1.111; 138-148,1.114; 208-225,1.103; 249-257,1.172;	ASN_GLYCOSYLATION 225-228; AMIDATION 10-13; MYRISTYL 217-222; ASN_GLYCOSYLATION 134-137; MYRISTYL 57-62; PKC_PHOSPHO_SITE 178-180; MYRISTYL 43-48; CAMP_PHOSPHO_SITE 119-122;	
DEX0455_061.aa.4	Y	0 - o1-133;	4-31,1.159; 61-129,1.207; 41-58,1.181;	ASN_GLYCOSYLATION 51-54; PKC_PHOSPHO_SITE 77-79;	
DEX0455_061.orf.5	N	0 - o1-163;	92-130,1.205; 56-85,1.181; 147-160,1.134; 4-11,1.118; 32-52,1.22;	CK2_PHOSPHO_SITE 51-54; MYRISTYL 17-22; PKC_PHOSPHO_SITE 5-7; CK2_PHOSPHO_SITE 47-50; MYRISTYL 143-148; MYRISTYL 144-149; MYRISTYL 139-144;	
DEX0455_062.aa.1	Y	0 - o1-491;	395-401,1.032; 180-196,1.118; 403-409,1.077; 121-138,1.121; 214-232,1.143; 4-31,1.234; 431-463,1.191; 259-269,1.1; 86-103,1.07; 292-308,1.304; 465-481,1.149; 69-84,1.2; 159-165,1.052;	CK2_PHOSPHO_SITE 22-25; MYRISTYL 140-145; CK2_PHOSPHO_SITE 290-293; CK2_PHOSPHO_SITE 315-318; CK2_PHOSPHO_SITE 343-346; PKC_PHOSPHO_SITE 157-159; MYRISTYL 422-427; CK2_PHOSPHO_SITE 257-260; MYRISTYL 454-459; CK2_PHOSPHO_SITE 405-408; PKC_PHOSPHO_SITE 100-102; CK2_PHOSPHO_SITE 158-161; CK2_PHOSPHO_SITE 248-251; MYRISTYL 401-406; CK2_PHOSPHO_SITE 375-378; MYRISTYL 90-95; PKC_PHOSPHO_SITE 464-466; PKC_PHOSPHO_SITE 106-108; MYRISTYL 116-121; PKC_PHOSPHO_SITE 158-160; MYRISTYL 105-110; PKC_PHOSPHO_SITE 148-150; MYRISTYL 79-84; MYRISTYL 19-24; MYRISTYL 458-463; MYRISTYL 144-149;	thiored 24-132; THIOREDOXIN 47-65; pdi_dom 165-269; THIOREDOXIN 189-198; THIOREDOXIN 46-54; THIOREDOXIN_2_2 161-284; THIOREDOXIN 233-244; THIOREDOXIN_2_1 26-137; thiored 159-270; pdi_dom 30-131; THIOREDOXIN 182-200;

			38-61,1.134; 201-207,1.072; 275-281,1.087; 369-375,1.067; 422-429,1.117; 316-326,1.166; 172-178,1.087;	PKC_PHOSPHO_SITE 239-241; MYRISTYL 7-12; CK2_PHOSPHO_SITE 23-26;	

Example 1b: Sequence Alignment Support

Alignments between previously identified sequences and splice variant sequences are performed to confirm unique portions of splice variant nucleic acid and amino acid sequences. The alignments are done using the Needle program in the European Molecular Biology Open Software Suite (EMBOSS) version 2.2.0 available at www.emboss.org from EMBnet (http://www.embnet.org). Default settings are used unless otherwise noted. The Needle program in EMBOSS implements the Needleman-Wunsch algorithm. Needleman, S. B., Wunsch, C. D., *J. Mol. Biol.* 48:443-453 (1970).

It is well know to those skilled in the art that implication of alignment algorithms by various programs may result in minor changes in the generated output. These changes include but are not limited to: alignment scores (percent identity, similarity, and gap), display of nonaligned flanking sequence regions, and number assignment to residues. These minor changes in the output of an alignment do not alter the physical characteristics of the sequences or the differences between the sequences, e.g. regions of homology, insertions, or deletions.

Example 1c: RT-PCR Analysis

To detect the presence and tissue distribution of a particular splice variant Reverse Transcription-Polymerase Chain Reaction (RT-PCR) is performed using cDNA generated from a panel of tissue RNAs. *See, e.g.*, Sambrook *et al.*, Molecular Cloning: A Laboratory Manual, 2d ed., Cold Spring Harbor Laboratory Press (1989) and; Kawasaki ES *et al.*, *PNAS* 85(15):5698 (1988). Total RNA is extracted from a variety of tissues and first strand cDNA is prepared with reverse transcriptase (RT). Each panel includes 23 cDNAs from five cancer types (lung, ovary, breast, colon, and prostate) and normal samples of

testis, placenta and fetal brain. Each cancer set is composed of three cancer cDNAs from different donors and one normal pooled sample. Using a standard enzyme kit from BD Bioscience Clontech (Mountain View, CA), the target transcript is detected with sequence-specific primers designed to only amplify the particular splice variant. The PCR reaction is run on the GeneAmp PCR system 9700 (Applied Biosystem, Foster City, CA) thermocycler under optimal conditions. One of ordinary skill can design appropriate primers and determine optimal conditions. The amplified product is resolved on an agarose gel to detect a band of equivalent size to the predicted RT-PCR product. A band indicated the presence of the splice variant in a sample. The relation of the amplified product to the splice variant was subsequently confirmed by DNA sequencing.

After subcloning, all positively screened clones are sequence verified. The DNA sequence verification results show the splice variant contains the predicted sequence differences in comparison with the reference sequence.

Results for RT-PCR analysis in the table below include the sequence DEX ID, Lead Name, Cancer Tissue(s) the transcript was detected in, Normal Tissue(s) the transcript was detected in, the predicted length of the RT-PCR product, and the confirmed Length of the RT-PCR product.

DEX ID	Lead Name	Cancer Tissue(s)	Normal Tissue(s)	Predicted Length	Confirmed Length
DEX0455_019.nt.1	Ovr224	Lung, Ovary, Colon, Prostate	Placenta, Fetal brain	334bp	334bp
DEX0455_034.nt.1, DEX0455_034.nt.2	Ovr223	Lung, Ovary, Breast, Colon		448bp	894bp (exon insertion)
DEX0455_034.nt.3	Ovr223v1	Lung, Ovary, Breast, Colon, Prostate	Lung, Breast, Colon, Prostate, Placenta	385bp	385bp
DEX0455_034.nt.4	Ovr223v2	Lung, Ovary, Breast, Colon, Prostate	Lung, Breast, Colon, Prostate, Placenta	491bp	491bp
DEX0455_037.nt.6	Ovr229	Ovary, Prostate	Prostate	390bp	387bp
DEX0455_037.nt.7	Ovr227	Prostate	Placenta	257bp	256bp
DEX0455_049.nt.1	Ovr232	Lung, Ovary, Breast, Colon	Breast	134bp	134bp

DEX0455_049.nt.2	Ovr232v1	Lung, Ovary, Breast, Colon, Prostate	Ovary, Breast	345bp	345bp
DEX0455_049.nt.3	Ovr232v2	Lung, Ovary, Breast, Colon, Prostate	Lung, Ovary, Breast, Colon, Prostate	334bp	334bp
DEX0455_049.nt.4	Ovr232v3	Colon	Breast	254bp	254bp
DEX0455_053.nt.2	Ovr110V1	Ovary, Breast, Prostate	Breast	383bp	383bp

RT-PCR results confirm the presence SEQ ID NO: 1-128 in biologic samples and distinguish between related transcripts.

Example 1d: Secretion Assay

To determine if a protein encoded by a splice variant is secreted from cells a secretion assay is preformed. A pcDNA3.1 clone containing the gene transcript which encodes the variant protein is transfected into 293T cells using the Superfect transfection reagent (Qiagen, Valencia CA). Transfected cells are incubated for 28 hours before the media is collected and immediately spun down to remove any detached cells. The adherent cells are solubilized with lysis buffer (1% NP40, 10mM sodium phosphate pH7.0, and 0.15M NaCl). The lysed cells are collected and spun down and the supernatant extracted as cell lysate. Western immunoblot is carried out in the following manner: 15µl of the cell lysate and media are run on 4-12% NuPage Bis-Tris gel (Invitrogen, Carlsbad CA), and blotted onto a PVDF membrane (Invitrogen, Carlsbad CA). The blot is incubated with a polyclonal primary antibody which binds to the variant protein (Imgenex, San Diego CA) and polyclonal goat anti-rabbit-peroxidase secondary antibody (Sigma-Aldrich, St. Louis MO). The blot is developed with the ECL Plus chemiluminescent detection reagent (Amersham BioSciences, Piscataway NJ).

Secretion assay results are indicative of SEQ ID NO: 129-295 being a diagnostic marker and/or therapeutic target for cancer.

Example 2a: Gene Expression Analysis

Custom Microarray Experiment - Cancer

Custom oligonucleotide microarrays were provided by Agilent Technologies, Inc. (Palo Alto, CA). The microarrays were fabricated by Agilent using their technology for

the *in-situ* synthesis of 60mer oligonucleotides (Hughes, et al. 2001, Nature Biotechnology 19:342-347). The 60mer microarray probes were designed by Agilent, from gene sequences provided by diaDexus, using Agilent proprietary algorithms. Whenever possible two different 60mers were designed for each gene of interest.

All microarray experiments were two-color experiments and were preformed using Agilent-recommended protocols and reagents. Briefly, each microarray was hybridized with cRNAs synthesized from RNA (total RNA for ovarian and prostate, polyA+ RNA for lung, breast and colon samples), isolated from cancer and normal tissues, labeled with fluorescent dyes Cyanine3 (Cy3) or Cyanine5 (Cy5) (NEN Life Science Products, Inc., Boston, MA) using a linear amplification method (Agilent). In each experiment the experimental sample was RNA isolated from cancer tissue from a single individual and the reference sample was a pool of RNA isolated from normal tissues of the same organ as the cancerous tissue (*i.e.* normal ovarian tissue in experiments with ovarian cancer samples). Hybridizations were carried out at 60°C, overnight using Agilent *in-situ* hybridization buffer. Following washing, arrays were scanned with a GenePix 4000B Microarray Scanner (Axon Instruments, Inc., Union City, CA). The resulting images were analyzed with GenePix Pro 3.0 Microarray Acquisition and Analysis Software (Axon).

Data normalization and expression profiling were done with Expressionist software from GeneData Inc. (Daly City, CA/Basel, Switzerland). Gene expression analysis was performed using only experiments that met certain quality criteria. The quality criteria that experiments must meet are a combination of evaluations performed by the Expressionist software and evaluations performed manually using raw and normalized data. To evaluate raw data quality, detection limits (the mean signal for a replicated negative control + 2 Standard Deviations (SD)) for each channel were calculated. The detection limit is a measure of non-specific hybridization. Acceptable detection limits were defined for each dye (<80 for Cy5 and <150 for Cy3). Arrays with poor detection limits in one or both channels were not analyzed and the experiments were repeated. To evaluate normalized data quality, positive control elements included in the array were utilized. These array features should have a mean ratio of 1 (no differential expression). If these features have a mean ratio of greater than 1.5-fold up or down, the experiments were not analyzed further and were repeated. In addition to traditional scatter plots demonstrating the distribution of signal in each experiment, the Expressionist software also has minimum thresholding criteria that employ user defined parameters to identify

quality data. These thresholds include two distinct quality measurements: 1) minimum area percentage, which is a measure of the integrity of each spot and 2) signal to noise ratio, which ensures that the signal being measured is significantly above any background (nonspecific) signal present. Only those features that met the threshold criteria were included in the filtering and analyses carried out by Expressionist. The thresholding settings employed require a minimum area percentage of 60% [(% pixels > background + 2SD)-(% pixels saturated)], and a minimum signal to noise ratio of 2.0 in both channels. By these criteria, very low expressors, saturated features and spots with abnormally high local background were not included in analysis.

Relative expression data was collected from Expressionist based on filtering and clustering analyses. Up-regulated genes were identified using criteria for the percentage of experiments in which the gene is up-regulated by at least 2-fold. In general, up-regulation in ~30% of samples tested was used as a cutoff for filtering.

Two microarray experiments were preformed for each normal and cancer tissue pair. The tissue specific Array Chip for each cancer tissue is a unique microarray specific to that tissue and cancer. The Multi-Cancer Array Chip is a universal microarray that was hybridized with samples from each of the cancers (ovarian, breast, colon, lung, and prostate). See the description below for the experiments specific to the different cancers.

Microarray Experiments and Data Tables

OVARIAN CANCER CHIPS

For ovarian cancer two different chip designs were evaluated with overlapping sets of a total of 19 samples, comparing the expression patterns of ovarian cancer derived total RNA to total RNA isolated from a pool of 9 normal ovarian tissues. For the Multi-Cancer Array Chip, all 19 samples (14 invasive carcinomas, 5 low malignant potential samples were analyzed and for the Ovarian Array Chip, a subset of 17 of these samples (13 invasive carcinomas, 4 low malignant potential samples) were assessed.

The results for the statistically significant up-regulated genes on the Ovarian Array Chip are shown in Table 1. The results for the Multi-Cancer Array Chip are shown in Table 2. The first two columns of each table contain information about the sequence itself (DEX ID, Oligo Name), the next columns show the results obtained for all ("ALL") ovarian cancer samples, invasive carcinomas ("INV") and low malignant potential ("LMP") samples. '%up' indicates the percentage of all experiments in which up-

regulation of at least 2-fold was observed (n=19 for the Multi-Cancer Array Chip, n=17 for the Ovarian Array Chip), '%valid up' indicates the percentage of experiments with valid expression values in which up-regulation of at least 2-fold was observed.

Table 1.

DEX ID	Oligo Name	Ovr ALL %up n=17	Ovr ALL %valid up n=17	Ovr INV %up n=13	Ovr INV %valid up n=13	Ovr LMP %up n=4	Ovr LMP %valid up n=4
DEX0455_001.nt.1	34930.01	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_001.nt.1	34930.02	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_002.nt.1	21553.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_002.nt.1	21553.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_002.nt.1	21577.01	17.6	20.0	15.4	16.7	25.0	33.3
DEX0455_002.nt.1	21577.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_003.nt.1	17466.01	11.8	11.8	7.7	7.7	25.0	25.0
DEX0455_003.nt.1	17466.02	11.8	11.8	7.7	7.7	25.0	25.0
DEX0455_005.nt.1	20619.01	23.5	25.0	23.1	23.1	25.0	33.3
DEX0455_005.nt.1	20619.02	17.6	20.0	15.4	16.7	25.0	33.3
DEX0455_005.nt.1	24874.01	23.5	25.0	23.1	25.0	25.0	25.0
DEX0455_005.nt.1	24874.02	29.4	31.2	23.1	25.0	50.0	50.0
DEX0455_005.nt.2	20619.01	23.5	25.0	23.1	23.1	25.0	33.3
DEX0455_005.nt.2	20619.02	17.6	20.0	15.4	16.7	25.0	33.3
DEX0455_005.nt.2	24874.01	23.5	25.0	23.1	25.0	25.0	25.0
DEX0455_005.nt.2	24874.02	29.4	31.2	23.1	25.0	50.0	50.0
DEX0455_007.nt.1	30109.01	41.2	46.7	30.8	33.3	75.0	100.0
DEX0455_007.nt.1	30109.02	35.3	40.0	23.1	27.3	75.0	75.0
DEX0455_008.nt.1	18508.01	23.5	44.4	30.8	44.4	0.0	0.0
DEX0455_008.nt.1	18508.02	17.6	23.1	23.1	30.0	0.0	0.0
DEX0455_008.nt.1	22387.01	35.3	54.5	46.2	66.7	0.0	0.0
DEX0455_008.nt.1	22387.02	41.2	43.8	53.8	58.3	0.0	0.0
DEX0455_009.nt.1	9720.01	47.1	47.1	38.5	38.5	75.0	75.0
DEX0455_009.nt.1	9720.02	52.9	52.9	46.2	46.2	75.0	75.0
DEX0455_010.nt.1	20627.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_010.nt.1	20627.02	23.5	25.0	23.1	25.0	25.0	25.0
DEX0455_010.nt.1	21675.01	11.8	11.8	15.4	15.4	0.0	0.0
DEX0455_010.nt.1	21675.02	11.8	11.8	15.4	15.4	0.0	0.0
DEX0455_010.nt.2	21675.01	11.8	11.8	15.4	15.4	0.0	0.0
DEX0455_010.nt.2	21675.02	11.8	11.8	15.4	15.4	0.0	0.0
DEX0455_013.nt.1	9838.01	35.3	42.9	38.5	45.5	25.0	33.3
DEX0455_013.nt.1	9838.02	35.3	37.5	38.5	38.5	25.0	33.3
DEX0455_013.nt.2	9838.01	35.3	42.9	38.5	45.5	25.0	33.3
DEX0455_013.nt.2	9838.02	35.3	37.5	38.5	38.5	25.0	33.3
DEX0455_014.nt.1	10624.01	17.6	50.0	15.4	50.0	25.0	50.0
DEX0455_014.nt.1	10624.02	17.6	50.0	7.7	33.3	50.0	66.7
DEX0455_014.nt.1	14604.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_014.nt.1	14604.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_015.nt.1	19518.01	29.4	29.4	38.5	38.5	0.0	0.0
DEX0455_015.nt.1	19518.02	29.4	29.4	38.5	38.5	0.0	0.0
DEX0455_016.nt.1	23734.01	5.9	6.2	7.7	7.7	0.0	0.0
DEX0455_016.nt.1	23734.02	11.8	11.8	15.4	15.4	0.0	0.0
DEX0455_018.nt.1	21571.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_018.nt.1	21571.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_018.nt.1	21575.01	41.2	41.2	46.2	46.2	25.0	25.0
DEX0455_018.nt.1	21575.02	41.2	41.2	46.2	46.2	25.0	25.0
DEX0455_018.nt.1	21609.01	0.0	0.0	0.0	0.0	0.0	0.0

DEX0455_018.nt.1	21609.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_018.nt.2	21575.01	41.2	41.2	46.2	46.2	25.0	25.0
DEX0455_018.nt.2	21575.02	41.2	41.2	46.2	46.2	25.0	25.0
DEX0455_019.nt.1	20669.01	35.3	42.9	46.2	50.0	0.0	0.0
DEX0455_019.nt.1	20669.02	35.3	46.2	46.2	50.0	0.0	0.0
DEX0455_021.nt.1	21433.01	64.7	64.7	61.5	61.5	75.0	75.0
DEX0455_021.nt.1	21433.02	64.7	64.7	61.5	61.5	75.0	75.0
DEX0455_021.nt.1	21469.01	70.6	70.6	61.5	61.5	100.0	100.0
DEX0455_021.nt.1	21469.02	82.4	82.4	76.9	76.9	100.0	100.0
DEX0455_021.nt.1	21475.01	58.8	58.8	53.8	53.8	75.0	75.0
DEX0455_021.nt.1	21475.02	52.9	52.9	53.8	53.8	50.0	50.0
DEX0455_021.nt.1	23780.01	47.1	47.1	46.2	46.2	50.0	50.0
DEX0455_021.nt.1	23780.02	41.2	50.0	46.2	54.5	25.0	33.3
DEX0455_021.nt.2	21433.01	64.7	64.7	61.5	61.5	75.0	75.0
DEX0455_021.nt.2	21433.02	64.7	64.7	61.5	61.5	75.0	75.0
DEX0455_021.nt.2	21469.01	70.6	70.6	61.5	61.5	100.0	100.0
DEX0455_021.nt.2	21469.02	82.4	82.4	76.9	76.9	100.0	100.0
DEX0455_021.nt.2	21475.01	58.8	58.8	53.8	53.8	75.0	75.0
DEX0455_021.nt.2	21475.02	52.9	52.9	53.8	53.8	50.0	50.0
DEX0455_021.nt.2	23780.01	47.1	47.1	46.2	46.2	50.0	50.0
DEX0455_021.nt.2	23780.02	41.2	50.0	46.2	54.5	25.0	33.3
DEX0455_021.nt.3	21433.01	64.7	64.7	61.5	61.5	75.0	75.0
DEX0455_021.nt.3	21433.02	64.7	64.7	61.5	61.5	75.0	75.0
DEX0455_021.nt.3	21469.01	70.6	70.6	61.5	61.5	100.0	100.0
DEX0455_021.nt.3	21469.02	82.4	82.4	76.9	76.9	100.0	100.0
DEX0455_021.nt.3	21475.01	58.8	58.8	53.8	53.8	75.0	75.0
DEX0455_021.nt.3	21475.02	52.9	52.9	53.8	53.8	50.0	50.0
DEX0455_021.nt.3	23780.01	47.1	47.1	46.2	46.2	50.0	50.0
DEX0455_021.nt.3	23780.02	41.2	50.0	46.2	54.5	25.0	33.3
DEX0455_021.nt.4	21433.01	64.7	64.7	61.5	61.5	75.0	75.0
DEX0455_021.nt.4	21433.02	64.7	64.7	61.5	61.5	75.0	75.0
DEX0455_021.nt.4	21469.01	70.6	70.6	61.5	61.5	100.0	100.0
DEX0455_021.nt.4	21469.02	82.4	82.4	76.9	76.9	100.0	100.0
DEX0455_021.nt.4	21475.01	58.8	58.8	53.8	53.8	75.0	75.0
DEX0455_021.nt.4	21475.02	52.9	52.9	53.8	53.8	50.0	50.0
DEX0455_021.nt.4	23780.01	47.1	47.1	46.2	46.2	50.0	50.0
DEX0455_021.nt.4	23780.02	41.2	50.0	46.2	54.5	25.0	33.3
DEX0455_022.nt.1	9920.01	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_022.nt.1	9920.02	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_022.nt.1	20299.01	17.6	18.8	23.1	25.0	0.0	0.0
DEX0455_022.nt.1	20299.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_022.nt.1	20311.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_022.nt.1	20311.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_022.nt.1	20317.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_022.nt.1	20317.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_022.nt.2	9920.01	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_022.nt.2	9920.02	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_022.nt.2	20299.01	17.6	18.8	23.1	25.0	0.0	0.0
DEX0455_022.nt.2	20299.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_022.nt.2	20311.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_022.nt.2	20311.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_022.nt.2	20317.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_022.nt.2	20317.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_022.nt.3	9920.01	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_022.nt.3	9920.02	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_022.nt.3	20311.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_022.nt.3	20311.02	17.6	17.6	23.1	23.1	0.0	0.0

DEX0455_022.nt.3	20317.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_022.nt.3	20317.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_023.nt.1	16187.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_023.nt.1	16187.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_023.nt.1	16374.01	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_023.nt.1	16374.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_023.nt.1	16378.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_023.nt.1	16378.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_024.nt.1	12149.01	52.9	52.9	46.2	46.2	75.0	75.0
DEX0455_024.nt.1	12149.02	47.1	47.1	38.5	38.5	75.0	75.0
DEX0455_024.nt.1	21487.01	5.9	6.7	7.7	8.3	0.0	0.0
DEX0455_024.nt.1	21487.02	17.6	18.8	15.4	16.7	25.0	25.0
DEX0455_024.nt.1	21507.01	29.4	29.4	23.1	23.1	50.0	50.0
DEX0455_024.nt.1	21507.02	29.4	31.2	23.1	25.0	50.0	50.0
DEX0455_024.nt.1	21547.01	47.1	47.1	46.2	46.2	50.0	50.0
DEX0455_024.nt.1	21547.02	41.2	41.2	38.5	38.5	50.0	50.0
DEX0455_024.nt.2	12149.01	52.9	52.9	46.2	46.2	75.0	75.0
DEX0455_024.nt.2	12149.02	47.1	47.1	38.5	38.5	75.0	75.0
DEX0455_024.nt.2	21507.01	29.4	29.4	23.1	23.1	50.0	50.0
DEX0455_024.nt.2	21507.02	29.4	31.2	23.1	25.0	50.0	50.0
DEX0455_024.nt.2	21547.01	47.1	47.1	46.2	46.2	50.0	50.0
DEX0455_024.nt.2	21547.02	41.2	41.2	38.5	38.5	50.0	50.0
DEX0455_025.nt.1	12167.01	17.6	18.8	23.1	23.1	0.0	0.0
DEX0455_025.nt.1	12167.02	11.8	11.8	15.4	15.4	0.0	0.0
DEX0455_025.nt.1	16956.01	5.9	5.9	7.7	7.7	0.0	0.0
DEX0455_025.nt.1	16956.02	5.9	5.9	7.7	7.7	0.0	0.0
DEX0455_025.nt.1	16958.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_025.nt.1	16958.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_025.nt.1	16964.01	5.9	5.9	7.7	7.7	0.0	0.0
DEX0455_025.nt.1	16964.02	5.9	5.9	7.7	7.7	0.0	0.0
DEX0455_025.nt.1	19010.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_025.nt.1	19010.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_025.nt.2	12167.01	17.6	18.8	23.1	23.1	0.0	0.0
DEX0455_025.nt.2	12167.02	11.8	11.8	15.4	15.4	0.0	0.0
DEX0455_025.nt.2	16956.01	5.9	5.9	7.7	7.7	0.0	0.0
DEX0455_025.nt.2	16956.02	5.9	5.9	7.7	7.7	0.0	0.0
DEX0455_025.nt.2	16958.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_025.nt.2	16958.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_025.nt.2	16964.01	5.9	5.9	7.7	7.7	0.0	0.0
DEX0455_025.nt.2	16964.02	5.9	5.9	7.7	7.7	0.0	0.0
DEX0455_025.nt.2	19010.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_025.nt.2	19010.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_025.nt.3	12167.01	17.6	18.8	23.1	23.1	0.0	0.0
DEX0455_025.nt.3	12167.02	11.8	11.8	15.4	15.4	0.0	0.0
DEX0455_025.nt.3	16958.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_025.nt.3	16958.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_025.nt.3	19010.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_025.nt.3	19010.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_025.nt.4	12167.01	17.6	18.8	23.1	23.1	0.0	0.0
DEX0455_025.nt.4	12167.02	11.8	11.8	15.4	15.4	0.0	0.0
DEX0455_025.nt.4	16956.01	5.9	5.9	7.7	7.7	0.0	0.0
DEX0455_025.nt.4	16956.02	5.9	5.9	7.7	7.7	0.0	0.0
DEX0455_025.nt.4	16958.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_025.nt.4	16958.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_025.nt.4	16964.01	5.9	5.9	7.7	7.7	0.0	0.0
DEX0455_025.nt.4	16964.02	5.9	5.9	7.7	7.7	0.0	0.0
DEX0455_025.nt.4	19010.01	0.0	0.0	0.0	0.0	0.0	0.0

DEX0455_025.nt.4	19010.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_027.nt.1	21549.01	29.4	31.2	23.1	25.0	50.0	50.0
DEX0455_027.nt.1	21549.02	29.4	31.2	23.1	25.0	50.0	50.0
DEX0455_029.nt.1	17430.01	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_029.nt.1	17430.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_029.nt.1	17448.01	11.8	11.8	15.4	15.4	0.0	0.0
DEX0455_029.nt.1	17448.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_029.nt.1	22113.01	11.8	25.0	15.4	28.6	0.0	0.0
DEX0455_029.nt.1	22113.02	11.8	20.0	15.4	25.0	0.0	0.0
DEX0455_029.nt.1	23386.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_029.nt.1	23386.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_029.nt.1	23400.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_029.nt.1	23400.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_029.nt.2	17424.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_029.nt.2	17424.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_029.nt.2	17430.01	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_029.nt.2	17430.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_029.nt.2	17448.01	11.8	11.8	15.4	15.4	0.0	0.0
DEX0455_029.nt.2	17448.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_029.nt.2	22113.01	11.8	25.0	15.4	28.6	0.0	0.0
DEX0455_029.nt.2	22113.02	11.8	20.0	15.4	25.0	0.0	0.0
DEX0455_029.nt.2	23386.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_029.nt.2	23386.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_029.nt.2	23400.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_029.nt.2	23400.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_030.nt.1	11613.01	11.8	11.8	15.4	15.4	0.0	0.0
DEX0455_030.nt.1	11613.02	11.8	13.3	15.4	16.7	0.0	0.0
DEX0455_030.nt.1	17204.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_030.nt.1	17204.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_030.nt.1	17262.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_030.nt.1	17262.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_030.nt.1	17278.01	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_030.nt.1	17278.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_030.nt.2	11613.01	11.8	11.8	15.4	15.4	0.0	0.0
DEX0455_030.nt.2	11613.02	11.8	13.3	15.4	16.7	0.0	0.0
DEX0455_030.nt.2	17204.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_030.nt.2	17204.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_030.nt.2	17262.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_030.nt.2	17262.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_030.nt.2	17274.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_030.nt.2	17274.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_030.nt.2	17278.01	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_030.nt.2	17278.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_031.nt.1	20773.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_031.nt.1	20773.02	23.5	25.0	30.8	33.3	0.0	0.0
DEX0455_031.nt.2	20773.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_031.nt.2	20773.02	23.5	25.0	30.8	33.3	0.0	0.0
DEX0455_031.nt.3	20773.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_031.nt.3	20773.02	23.5	25.0	30.8	33.3	0.0	0.0
DEX0455_032.nt.1	11585.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_032.nt.1	11585.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_032.nt.1	18556.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_032.nt.1	18556.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_034.nt.1	10722.01	82.4	82.4	84.6	84.6	75.0	75.0
DEX0455_034.nt.1	10722.02	76.5	81.2	84.6	84.6	50.0	66.7
DEX0455_034.nt.1	21401.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_034.nt.1	21401.02	5.9	6.7	7.7	8.3	0.0	0.0

DEX0455_034.nt.1	21421.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_034.nt.1	21421.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_035.nt.1	103385.01	58.8	58.8	76.9	76.9	0.0	0.0
DEX0455_035.nt.1	103385.02	58.8	58.8	76.9	76.9	0.0	0.0
DEX0455_035.nt.2	103385.01	58.8	58.8	76.9	76.9	0.0	0.0
DEX0455_035.nt.2	103385.02	58.8	58.8	76.9	76.9	0.0	0.0
DEX0455_035.nt.3	103385.01	58.8	58.8	76.9	76.9	0.0	0.0
DEX0455_035.nt.3	103385.02	58.8	58.8	76.9	76.9	0.0	0.0
DEX0455_036.nt.1	92327.01	52.9	56.2	61.5	66.7	25.0	25.0
DEX0455_036.nt.1	92327.02	52.9	52.9	61.5	61.5	25.0	25.0
DEX0455_036.nt.2	92327.01	52.9	56.2	61.5	66.7	25.0	25.0
DEX0455_036.nt.2	92327.02	52.9	52.9	61.5	61.5	25.0	25.0
DEX0455_036.nt.3	92327.01	52.9	56.2	61.5	66.7	25.0	25.0
DEX0455_036.nt.3	92327.02	52.9	52.9	61.5	61.5	25.0	25.0
DEX0455_036.nt.4	92327.01	52.9	56.2	61.5	66.7	25.0	25.0
DEX0455_036.nt.4	92327.02	52.9	52.9	61.5	61.5	25.0	25.0
DEX0455_037.nt.1	11575.01	52.9	52.9	53.8	53.8	50.0	50.0
DEX0455_037.nt.1	11575.02	52.9	52.9	53.8	53.8	50.0	50.0
DEX0455_037.nt.1	17486.01	47.1	47.1	46.2	46.2	50.0	50.0
DEX0455_037.nt.1	17486.02	47.1	47.1	46.2	46.2	50.0	50.0
DEX0455_037.nt.1	17490.01	52.9	52.9	53.8	53.8	50.0	50.0
DEX0455_037.nt.1	17490.02	58.8	58.8	53.8	53.8	75.0	75.0
DEX0455_037.nt.2	11575.01	52.9	52.9	53.8	53.8	50.0	50.0
DEX0455_037.nt.2	11575.02	52.9	52.9	53.8	53.8	50.0	50.0
DEX0455_037.nt.2	17486.01	47.1	47.1	46.2	46.2	50.0	50.0
DEX0455_037.nt.2	17486.02	47.1	47.1	46.2	46.2	50.0	50.0
DEX0455_037.nt.2	17490.01	52.9	52.9	53.8	53.8	50.0	50.0
DEX0455_037.nt.2	17490.02	58.8	58.8	53.8	53.8	75.0	75.0
DEX0455_037.nt.3	11575.01	52.9	52.9	53.8	53.8	50.0	50.0
DEX0455_037.nt.3	11575.02	52.9	52.9	53.8	53.8	50.0	50.0
DEX0455_037.nt.3	17486.01	47.1	47.1	46.2	46.2	50.0	50.0
DEX0455_037.nt.3	17486.02	47.1	47.1	46.2	46.2	50.0	50.0
DEX0455_037.nt.3	17490.01	52.9	52.9	53.8	53.8	50.0	50.0
DEX0455_037.nt.3	17490.02	58.8	58.8	53.8	53.8	75.0	75.0
DEX0455_037.nt.4	11575.01	52.9	52.9	53.8	53.8	50.0	50.0
DEX0455_037.nt.4	11575.02	52.9	52.9	53.8	53.8	50.0	50.0
DEX0455_037.nt.4	17486.01	47.1	47.1	46.2	46.2	50.0	50.0
DEX0455_037.nt.4	17486.02	47.1	47.1	46.2	46.2	50.0	50.0
DEX0455_037.nt.4	17490.01	52.9	52.9	53.8	53.8	50.0	50.0
DEX0455_037.nt.4	17490.02	58.8	58.8	53.8	53.8	75.0	75.0
DEX0455_037.nt.5	11575.01	52.9	52.9	53.8	53.8	50.0	50.0
DEX0455_037.nt.5	11575.02	52.9	52.9	53.8	53.8	50.0	50.0
DEX0455_037.nt.5	17486.01	47.1	47.1	46.2	46.2	50.0	50.0
DEX0455_037.nt.5	17486.02	47.1	47.1	46.2	46.2	50.0	50.0
DEX0455_037.nt.5	17490.01	52.9	52.9	53.8	53.8	50.0	50.0
DEX0455_037.nt.5	17490.02	58.8	58.8	53.8	53.8	75.0	75.0
DEX0455_039.nt.1	21505.01	94.1	94.1	92.3	92.3	100.0	100.0
DEX0455_039.nt.1	21505.02	94.1	94.1	92.3	92.3	100.0	100.0
DEX0455_039.nt.2	11527.01	88.2	88.2	84.6	84.6	100.0	100.0
DEX0455_039.nt.2	11527.02	88.2	88.2	84.6	84.6	100.0	100.0
DEX0455_040.nt.1	21489.01	11.8	11.8	15.4	15.4	0.0	0.0
DEX0455_040.nt.1	21489.02	17.6	18.8	23.1	23.1	0.0	0.0
DEX0455_040.nt.1	21501.01	47.1	50.0	61.5	61.5	0.0	0.0
DEX0455_040.nt.1	21501.02	41.2	41.2	53.8	53.8	0.0	0.0
DEX0455_040.nt.1	21511.01	47.1	47.1	61.5	61.5	0.0	0.0
DEX0455_040.nt.1	21511.02	47.1	47.1	53.8	53.8	25.0	25.0
DEX0455_040.nt.2	21489.01	11.8	11.8	15.4	15.4	0.0	0.0

DEX0455_040.nt.2	21489.02	17.6	18.8	23.1	23.1	0.0	0.0
DEX0455_040.nt.2	21501.01	47.1	50.0	61.5	61.5	0.0	0.0
DEX0455_040.nt.2	21501.02	41.2	41.2	53.8	53.8	0.0	0.0
DEX0455_040.nt.2	21511.01	47.1	47.1	61.5	61.5	0.0	0.0
DEX0455_040.nt.2	21511.02	47.1	47.1	53.8	53.8	25.0	25.0
DEX0455_041.nt.1	12155.01	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_041.nt.1	12155.02	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_041.nt.1	16980.01	29.4	29.4	38.5	38.5	0.0	0.0
DEX0455_041.nt.1	16980.02	29.4	29.4	38.5	38.5	0.0	0.0
DEX0455_041.nt.2	12155.01	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_041.nt.2	12155.02	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_042.nt.1	18214.01	94.1	94.1	92.3	92.3	100.0	100.0
DEX0455_042.nt.1	18214.02	88.2	93.8	84.6	91.7	100.0	100.0
DEX0455_043.nt.1	14656.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_043.nt.1	14656.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_043.nt.3	14656.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_043.nt.3	14656.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_045.nt.1	36013.01	23.5	23.5	7.7	7.7	75.0	75.0
DEX0455_045.nt.1	36013.02	11.8	11.8	0.0	0.0	50.0	50.0
DEX0455_046.nt.1	17314.01	23.5	26.7	15.4	16.7	50.0	66.7
DEX0455_046.nt.1	17314.02	23.5	26.7	15.4	16.7	50.0	66.7
DEX0455_049.nt.1	11511.01	94.1	100.0	92.3	100.0	100.0	100.0
DEX0455_049.nt.1	11511.02	88.2	100.0	84.6	100.0	100.0	100.0
DEX0455_049.nt.2	11511.01	94.1	100.0	92.3	100.0	100.0	100.0
DEX0455_049.nt.2	11511.02	88.2	100.0	84.6	100.0	100.0	100.0
DEX0455_049.nt.4	11511.01	94.1	100.0	92.3	100.0	100.0	100.0
DEX0455_049.nt.4	11511.02	88.2	100.0	84.6	100.0	100.0	100.0
DEX0455_049.nt.5	11511.01	94.1	100.0	92.3	100.0	100.0	100.0
DEX0455_049.nt.5	11511.02	88.2	100.0	84.6	100.0	100.0	100.0
DEX0455_050.nt.1	23378.01	11.8	18.2	15.4	20.0	0.0	0.0
DEX0455_050.nt.1	23378.02	17.6	23.1	7.7	9.1	50.0	100.0
DEX0455_052.nt.1	91971.01	94.1	94.1	92.3	92.3	100.0	100.0
DEX0455_052.nt.1	91971.02	94.1	94.1	92.3	92.3	100.0	100.0
DEX0455_055.nt.1	11273.01	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_055.nt.1	11273.02	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_055.nt.1	20541.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_055.nt.1	20541.02	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_055.nt.2	11273.01	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_055.nt.2	11273.02	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_055.nt.2	20541.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_055.nt.2	20541.02	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_055.nt.3	11273.01	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_055.nt.3	11273.02	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_055.nt.3	20541.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_055.nt.3	20541.02	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_056.nt.1	18520.01	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_056.nt.1	18520.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_056.nt.1	22734.01	5.9	5.9	7.7	7.7	0.0	0.0
DEX0455_056.nt.1	22734.02	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_056.nt.1	23444.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_056.nt.1	23444.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_056.nt.2	18520.01	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_056.nt.2	18520.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_056.nt.2	22734.01	5.9	5.9	7.7	7.7	0.0	0.0
DEX0455_056.nt.2	22734.02	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_056.nt.2	23444.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_056.nt.2	23444.02	0.0	0.0	0.0	0.0	0.0	0.0

DEX0455_057.nt.1	24524.01	70.6	70.6	69.2	69.2	75.0	75.0
DEX0455_057.nt.1	24524.02	70.6	70.6	69.2	69.2	75.0	75.0
DEX0455_057.nt.2	24524.01	70.6	70.6	69.2	69.2	75.0	75.0
DEX0455_057.nt.2	24524.02	70.6	70.6	69.2	69.2	75.0	75.0
DEX0455_058.nt.1	14656.01	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_058.nt.1	14656.02	17.6	17.6	23.1	23.1	0.0	0.0
DEX0455_059.nt.1	11469.01	47.1	47.1	61.5	61.5	0.0	0.0
DEX0455_059.nt.1	11469.02	52.9	52.9	61.5	61.5	25.0	25.0
DEX0455_059.nt.1	17370.01	5.9	25.0	7.7	25.0	0.0	0.0
DEX0455_059.nt.1	17370.02	5.9	25.0	7.7	25.0	0.0	0.0
DEX0455_059.nt.1	17372.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_059.nt.1	17372.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_059.nt.2	11469.01	47.1	47.1	61.5	61.5	0.0	0.0
DEX0455_059.nt.2	11469.02	52.9	52.9	61.5	61.5	25.0	25.0
DEX0455_059.nt.2	17372.01	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_059.nt.2	17372.02	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_060.nt.1	10372.01	35.3	35.3	46.2	46.2	0.0	0.0
DEX0455_060.nt.1	10372.02	35.3	35.3	46.2	46.2	0.0	0.0
DEX0455_060.nt.1	18582.01	23.5	23.5	30.8	30.8	0.0	0.0
DEX0455_060.nt.1	18582.02	29.4	29.4	38.5	38.5	0.0	0.0
DEX0455_061.nt.1	96523.01	23.5	23.5	15.4	15.4	50.0	50.0
DEX0455_061.nt.1	96523.02	17.6	17.6	7.7	7.7	50.0	50.0
DEX0455_061.nt.1	103529.01	23.5	25.0	15.4	16.7	50.0	50.0
DEX0455_061.nt.1	103529.02	23.5	23.5	15.4	15.4	50.0	50.0
DEX0455_061.nt.2	96523.01	23.5	23.5	15.4	15.4	50.0	50.0
DEX0455_061.nt.2	96523.02	17.6	17.6	7.7	7.7	50.0	50.0
DEX0455_061.nt.2	103529.01	23.5	25.0	15.4	16.7	50.0	50.0
DEX0455_061.nt.2	103529.02	23.5	23.5	15.4	15.4	50.0	50.0
DEX0455_061.nt.3	96523.01	23.5	23.5	15.4	15.4	50.0	50.0
DEX0455_061.nt.3	96523.02	17.6	17.6	7.7	7.7	50.0	50.0
DEX0455_061.nt.3	103529.01	23.5	25.0	15.4	16.7	50.0	50.0
DEX0455_061.nt.3	103529.02	23.5	23.5	15.4	15.4	50.0	50.0
DEX0455_061.nt.4	96523.01	23.5	23.5	15.4	15.4	50.0	50.0
DEX0455_061.nt.4	96523.02	17.6	17.6	7.7	7.7	50.0	50.0
DEX0455_061.nt.4	103529.01	23.5	25.0	15.4	16.7	50.0	50.0
DEX0455_061.nt.4	103529.02	23.5	23.5	15.4	15.4	50.0	50.0
DEX0455_061.nt.5	96523.01	23.5	23.5	15.4	15.4	50.0	50.0
DEX0455_061.nt.5	96523.02	17.6	17.6	7.7	7.7	50.0	50.0
DEX0455_061.nt.5	103529.01	23.5	25.0	15.4	16.7	50.0	50.0
DEX0455_061.nt.5	103529.02	23.5	23.5	15.4	15.4	50.0	50.0
DEX0455_062.nt.1	17464.01	29.4	29.4	38.5	38.5	0.0	0.0
DEX0455_062.nt.1	17464.02	29.4	29.4	38.5	38.5	0.0	0.0
DEX0455_062.nt.1	18094.01	52.9	52.9	69.2	69.2	0.0	0.0
DEX0455_062.nt.1	18094.02	52.9	52.9	69.2	69.2	0.0	0.0

Table 2.

DEX ID	Oligo Name	Ovr Multi-Cancer ALL %up n=19	Ovr Multi-Cancer ALL %valid up n=19	Ovr Multi-Cancer INV %up n=14	Ovr Multi-Cancer INV %valid up n=14	Ovr Multi-Cancer LMP %up n=5	Ovr Multi-Cancer LMP %valid up n=5
DEX0455_002.nt.1	79699.1	10.5	10.5	14.3	14.3	0.0	0.0
DEX0455_002.nt.1	79700.0	10.5	10.5	14.3	14.3	0.0	0.0
DEX0455_002.nt.1	79700.1	26.3	26.3	21.4	21.4	40.0	40.0
DEX0455_004.nt.1	96339.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	96339.1	0.0	0.0	0.0	0.0	0.0	0.0

DEX0455_004.nt.1	96340.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	96340.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105991.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105991.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105992.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105992.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105996.0	21.1	21.1	28.6	28.6	0.0	0.0
DEX0455_004.nt.1	105996.1	21.1	21.1	28.6	28.6	0.0	0.0
DEX0455_004.nt.2	96339.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	96339.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	96340.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	96340.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105991.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105991.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105992.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105992.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105996.0	21.1	21.1	28.6	28.6	0.0	0.0
DEX0455_004.nt.2	105996.1	21.1	21.1	28.6	28.6	0.0	0.0
DEX0455_011.nt.1	35317.0	31.6	42.9	14.3	20.0	80.0	100.0
DEX0455_011.nt.1	35317.1	31.6	35.3	14.3	15.4	80.0	100.0
DEX0455_012.nt.1	34334.0	89.5	89.5	85.7	85.7	100.0	100.0
DEX0455_012.nt.1	34334.1	84.2	88.9	85.7	85.7	80.0	100.0
DEX0455_012.nt.1	34335.0	94.7	100.0	92.9	100.0	100.0	100.0
DEX0455_012.nt.1	34335.1	89.5	100.0	92.9	100.0	80.0	100.0
DEX0455_012.nt.2	34334.0	89.5	89.5	85.7	85.7	100.0	100.0
DEX0455_012.nt.2	34334.1	84.2	88.9	85.7	85.7	80.0	100.0
DEX0455_012.nt.2	34335.0	94.7	100.0	92.9	100.0	100.0	100.0
DEX0455_012.nt.2	34335.1	89.5	100.0	92.9	100.0	80.0	100.0
DEX0455_017.nt.1	36482.0	31.6	42.9	28.6	40.0	40.0	50.0
DEX0455_017.nt.1	36482.1	31.6	50.0	28.6	44.4	40.0	66.7
DEX0455_033.nt.1	2023.0	21.1	23.5	28.6	30.8	0.0	0.0
DEX0455_033.nt.1	5327.0	15.8	16.7	21.4	21.4	0.0	0.0
DEX0455_033.nt.1	5328.0	10.5	11.1	14.3	14.3	0.0	0.0
DEX0455_035.nt.1	78519.0	42.1	47.1	57.1	57.1	0.0	0.0
DEX0455_035.nt.1	78519.1	47.4	52.9	64.3	69.2	0.0	0.0
DEX0455_035.nt.1	78520.0	36.8	38.9	50.0	50.0	0.0	0.0
DEX0455_035.nt.1	78520.1	42.1	44.4	57.1	57.1	0.0	0.0
DEX0455_035.nt.2	78519.0	42.1	47.1	57.1	57.1	0.0	0.0
DEX0455_035.nt.2	78519.1	47.4	52.9	64.3	69.2	0.0	0.0
DEX0455_035.nt.2	78520.0	36.8	38.9	50.0	50.0	0.0	0.0
DEX0455_035.nt.2	78520.1	42.1	44.4	57.1	57.1	0.0	0.0
DEX0455_035.nt.3	78519.0	42.1	47.1	57.1	57.1	0.0	0.0
DEX0455_035.nt.3	78519.1	47.4	52.9	64.3	69.2	0.0	0.0
DEX0455_035.nt.3	78520.0	36.8	38.9	50.0	50.0	0.0	0.0
DEX0455_035.nt.3	78520.1	42.1	44.4	57.1	57.1	0.0	0.0
DEX0455_038.nt.1	23542.0	5.3	5.6	7.1	7.7	0.0	0.0
DEX0455_038.nt.1	23542.1	10.5	10.5	14.3	14.3	0.0	0.0
DEX0455_038.nt.1	23543.0	15.8	16.7	14.3	15.4	20.0	20.0
DEX0455_038.nt.1	23543.1	21.1	21.1	21.4	21.4	20.0	20.0
DEX0455_038.nt.2	23542.0	5.3	5.6	7.1	7.7	0.0	0.0
DEX0455_038.nt.2	23542.1	10.5	10.5	14.3	14.3	0.0	0.0
DEX0455_038.nt.2	23543.0	15.8	16.7	14.3	15.4	20.0	20.0
DEX0455_038.nt.2	23543.1	21.1	21.1	21.4	21.4	20.0	20.0
DEX0455_038.nt.3	23542.0	5.3	5.6	7.1	7.7	0.0	0.0
DEX0455_038.nt.3	23542.1	10.5	10.5	14.3	14.3	0.0	0.0
DEX0455_038.nt.3	23543.0	15.8	16.7	14.3	15.4	20.0	20.0
DEX0455_038.nt.3	23543.1	21.1	21.1	21.4	21.4	20.0	20.0

DEX0455_047.nt.1	96212.0	10.5	11.8	14.3	15.4	0.0	0.0
DEX0455_047.nt.1	96212.1	5.3	5.9	7.1	7.7	0.0	0.0
DEX0455_047.nt.1	105764.0	10.5	12.5	14.3	15.4	0.0	0.0
DEX0455_047.nt.1	105764.1	15.8	16.7	14.3	15.4	20.0	20.0
DEX0455_047.nt.1	105767.0	15.8	15.8	14.3	14.3	20.0	20.0
DEX0455_047.nt.1	105767.1	15.8	15.8	14.3	14.3	20.0	20.0
DEX0455_047.nt.1	105768.0	15.8	15.8	14.3	14.3	20.0	20.0
DEX0455_047.nt.1	105768.1	21.1	22.2	21.4	23.1	20.0	20.0
DEX0455_047.nt.2	96212.0	10.5	11.8	14.3	15.4	0.0	0.0
DEX0455_047.nt.2	96212.1	5.3	5.9	7.1	7.7	0.0	0.0
DEX0455_047.nt.2	105764.0	10.5	12.5	14.3	15.4	0.0	0.0
DEX0455_047.nt.2	105764.1	15.8	16.7	14.3	15.4	20.0	20.0
DEX0455_047.nt.2	105767.0	15.8	15.8	14.3	14.3	20.0	20.0
DEX0455_047.nt.2	105767.1	15.8	15.8	14.3	14.3	20.0	20.0
DEX0455_047.nt.2	105768.0	15.8	15.8	14.3	14.3	20.0	20.0
DEX0455_047.nt.2	105768.1	21.1	22.2	21.4	23.1	20.0	20.0
DEX0455_048.nt.1	1168.0	10.5	10.5	14.3	14.3	0.0	0.0
DEX0455_048.nt.2	1175.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23378.0	5.3	5.3	7.1	7.1	0.0	0.0
DEX0455_050.nt.1	23378.1	5.3	5.3	7.1	7.1	0.0	0.0
DEX0455_050.nt.1	23379.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23379.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42007.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42007.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42007.2	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42008.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42008.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42008.2	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_061.nt.1	78508.0	21.1	21.1	21.4	21.4	20.0	20.0
DEX0455_061.nt.1	78508.1	21.1	21.1	21.4	21.4	20.0	20.0
DEX0455_061.nt.2	78508.0	21.1	21.1	21.4	21.4	20.0	20.0
DEX0455_061.nt.2	78508.1	21.1	21.1	21.4	21.4	20.0	20.0
DEX0455_061.nt.3	78508.0	21.1	21.1	21.4	21.4	20.0	20.0
DEX0455_061.nt.3	78508.1	21.1	21.1	21.4	21.4	20.0	20.0
DEX0455_061.nt.4	78508.0	21.1	21.1	21.4	21.4	20.0	20.0
DEX0455_061.nt.4	78508.1	21.1	21.1	21.4	21.4	20.0	20.0
DEX0455_061.nt.5	78508.0	21.1	21.1	21.4	21.4	20.0	20.0
DEX0455_061.nt.5	78508.1	21.1	21.1	21.4	21.4	20.0	20.0

BREAST CANCER CHIPS

For breast cancer two different chip designs were evaluated with overlapping sets of a total of 36 samples, comparing the expression patterns of breast cancer derived polyA+ RNA to polyA+ RNA isolated from a pool of 10 normal breast tissues. For the Breast Array Chip, all 36 samples (9 stage I cancers, 23 stage II cancers, 4 stage III cancers) were analyzed. These samples also represented 10 Grade1/2 and 26 Grade 3 cancers. The histopathologic grades for cancer are classified as follows: GX, cannot be assessed; G1, well differentiated; G2, moderately differentiated; G3, poorly differentiated; and G4, undifferentiated. AJCC Cancer Staging Handbook, pp. 9, (5th Ed, 1998). Samples were further grouped based on the expression patterns of the known breast cancer

associated genes Her2 and ERα (10 HER2 up, 26 HER2 not up, 20 ER up and 16 ER not up) and for the Multi-Cancer Array Chip, a subset of 20 of these samples (9 stage I cancers, 8 stage II cancers, 3 stage III cancers) were assessed.

The results for the statistically significant up-regulated genes on the Breast Array Chip are shown in Tables 3 and 4. The results for the statistically significant up-regulated genes on the Multi-Cancer Array Chip are shown in Table 5. The first two columns of each table contain information about the sequence itself (Seq ID, Oligo Name), the next columns show the results obtained for all ("ALL") breast cancer samples, cancers corresponding to stageI ("ST1"), stages II and III ("ST2,3"), grades 1 and 2 ("GR1,2"), grade 3 ("GR3"), cancers exhibiting up-regulation of Her2 ("HER2up") or ERα ("ERup") or those not exhibiting up-regulation of Her2 ("NOT HER2up") or ERα ("NOT ERup"). '%up' indicates the percentage of all experiments in which up-regulation of at least 2-fold was observed (n=36 for Colon Array Chip, n=20 for the Multi-Cancer Array Chip), '%valid up' indicates the percentage of experiments with valid expression values in which up-regulation of at least 2-fold was observed.

Table 3.

DEX ID	Oligo Name	Mam ALL %up n=36	Mam ALL % valid up n=36	Mam ST1 %up n=9	Mam ST1 % valid up n=9	Mam ST2,3 %up n=27	Mam ST2,3 % valid up n=27	Mam GR1,2 %up n=10	Mam GR1,2 % valid up n=10	Mam GR3 %up n=26	Mam GR3 % valid up n=26
DEX0455_010.nt.1	32151.0	22.2	22.2	44.4	44.4	14.8	14.8	10.0	10.0	26.9	26.9
DEX0455_017.nt.1	28221.0	2.8	3.1	0.0	0.0	3.7	4.3	0.0	0.0	3.8	4.5
DEX0455_022.nt.1	23280.0	11.1	11.8	11.1	11.1	11.1	12.0	10.0	10.0	11.5	12.5
DEX0455_035.nt.3	21143.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_035.nt.3	21144.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_041.nt.1	16998.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_046.nt.1	19072.0	11.1	11.4	0.0	0.0	14.8	15.4	20.0	20.0	7.7	8.0
DEX0455_050.nt.1	22136.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23378.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23378.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23379.0	5.6	5.7	0.0	0.0	7.4	7.7	0.0	0.0	7.7	8.0
DEX0455_050.nt.1	23379.2	5.6	5.7	0.0	0.0	7.4	7.7	0.0	0.0	7.7	8.0

DEX0455_050.nt.1	29736.0	2.8	2.8	0.0	0.0	3.7	3.7	0.0	0.0	3.8	3.8
DEX0455_054.nt.1	19799.0	8.3	8.3	0.0	0.0	11.1	11.1	0.0	0.0	11.5	11.5
DEX0455_055.nt.1	12731.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_055.nt.1	12732.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_055.nt.2	12731.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_055.nt.2	12732.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_055.nt.3	12731.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_055.nt.3	12732.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Table 4.

DEX ID	Oligo Name	Mam HER2up %up n=10	Mam HER2up %valid up n=10	Mam NOT HER2up %up n=26	Mam NOT HER2up %valid up n=26	Mam ERup %up n=20	Mam ERup %valid up n=20	Mam NOT ERup %up n=16	Mam NOT ERup %valid up n=16
DEX0455_010.nt.1	32151.0	20.0	20.0	23.1	23.1	10.0	10.0	37.5	37.5
DEX0455_017.nt.1	28221.0	10.0	11.1	0.0	0.0	0.0	0.0	6.2	8.3
DEX0455_022.nt.1	23280.0	20.0	20.0	7.7	8.3	10.0	11.1	12.5	12.5
DEX0455_035.nt.3	21143.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_035.nt.3	21144.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_041.nt.1	16998.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_046.nt.1	19072.0	20.0	20.0	7.7	8.0	15.0	15.0	6.2	6.7
DEX0455_050.nt.1	22136.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23378.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23378.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23379.0	0.0	0.0	7.7	8.0	0.0	0.0	12.5	13.3
DEX0455_050.nt.1	23379.2	0.0	0.0	7.7	8.0	0.0	0.0	12.5	13.3
DEX0455_050.nt.1	29736.0	0.0	0.0	3.8	3.8	0.0	0.0	6.2	6.2
DEX0455_054.nt.1	19799.0	10.0	10.0	7.7	7.7	10.0	10.0	6.2	6.2
DEX0455_055.nt.1	12731.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_055.nt.1	12732.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_055.nt.2	12731.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_055.nt.2	12732.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_055.nt.3	12731.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_055.nt.3	12732.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Table 5.

DEX ID	Oligo Name	Mam Multi-Cancer ALL %up n=20	Mam Multi-Cancer ALL %valid up n=20	Mam Multi-Cancer ST1 %up n=9	Mam Multi-Cancer ST1 %valid up n=9	Mam Multi-Cancer ST2,3 %up n=11	Mam Multi-Cancer ST2,3 %valid up n=11
DEX0455_002.nt.1	79699.1	20.0	20.0	44.4	44.4	0.0	0.0
DEX0455_002.nt.1	79700.0	10.0	10.0	22.2	22.2	0.0	0.0
DEX0455_002.nt.1	79700.1	15.0	15.0	33.3	33.3	0.0	0.0
DEX0455_004.nt.1	96339.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	96339.1	0.0	0.0	0.0	0.0	0.0	0.0

DEX0455_004.nt.1	96340.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	96340.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105991.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105991.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105992.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105992.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105996.0	15.0	15.0	11.1	11.1	18.2	18.2
DEX0455_004.nt.1	105996.1	15.0	15.0	11.1	11.1	18.2	18.2
DEX0455_004.nt.2	96339.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	96339.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	96340.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	96340.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105991.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105991.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105992.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105992.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105996.0	15.0	15.0	11.1	11.1	18.2	18.2
DEX0455_004.nt.2	105996.1	15.0	15.0	11.1	11.1	18.2	18.2
DEX0455_011.nt.1	35317.0	5.0	7.1	11.1	20.0	0.0	0.0
DEX0455_011.nt.1	35317.1	5.0	7.1	11.1	20.0	0.0	0.0
DEX0455_012.nt.1	34334.0	5.0	5.0	0.0	0.0	9.1	9.1
DEX0455_012.nt.1	34334.1	5.0	5.0	0.0	0.0	9.1	9.1
DEX0455_012.nt.1	34335.0	5.0	5.0	0.0	0.0	9.1	9.1
DEX0455_012.nt.1	34335.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_012.nt.2	34334.0	5.0	5.0	0.0	0.0	9.1	9.1
DEX0455_012.nt.2	34334.1	5.0	5.0	0.0	0.0	9.1	9.1
DEX0455_012.nt.2	34335.0	5.0	5.0	0.0	0.0	9.1	9.1
DEX0455_012.nt.2	34335.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_017.nt.1	36482.0	10.0	10.0	11.1	11.1	9.1	9.1
DEX0455_017.nt.1	36482.1	10.0	10.0	11.1	11.1	9.1	9.1
DEX0455_033.nt.1	2023.0	10.0	10.0	0.0	0.0	18.2	18.2
DEX0455_033.nt.1	5327.0	10.0	10.0	0.0	0.0	18.2	18.2
DEX0455_033.nt.1	5328.0	10.0	10.0	0.0	0.0	18.2	18.2
DEX0455_035.nt.1	78519.0	50.0	50.0	66.7	66.7	36.4	36.4
DEX0455_035.nt.1	78519.1	40.0	40.0	66.7	66.7	18.2	18.2
DEX0455_035.nt.1	78520.0	20.0	20.0	33.3	33.3	9.1	9.1
DEX0455_035.nt.1	78520.1	20.0	20.0	33.3	33.3	9.1	9.1
DEX0455_035.nt.2	78519.0	50.0	50.0	66.7	66.7	36.4	36.4
DEX0455_035.nt.2	78519.1	40.0	40.0	66.7	66.7	18.2	18.2
DEX0455_035.nt.2	78520.0	20.0	20.0	33.3	33.3	9.1	9.1
DEX0455_035.nt.2	78520.1	20.0	20.0	33.3	33.3	9.1	9.1
DEX0455_035.nt.3	78519.0	50.0	50.0	66.7	66.7	36.4	36.4
DEX0455_035.nt.3	78519.1	40.0	40.0	66.7	66.7	18.2	18.2
DEX0455_035.nt.3	78520.0	20.0	20.0	33.3	33.3	9.1	9.1
DEX0455_035.nt.3	78520.1	20.0	20.0	33.3	33.3	9.1	9.1
DEX0455_038.nt.1	23542.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	23542.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	23543.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	23543.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	23542.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	23542.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	23543.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	23543.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.3	23542.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.3	23542.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.3	23543.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.3	23543.1	0.0	0.0	0.0	0.0	0.0	0.0

DEX0455_047.nt.1	96212.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	96212.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	105764.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	105764.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	105767.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	105767.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	105768.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	105768.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	96212.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	96212.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	105764.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	105764.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	105767.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	105767.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	105768.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	105768.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_048.nt.1	1168.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_048.nt.2	1175.0	5.0	5.0	0.0	0.0	9.1	9.1
DEX0455_050.nt.1	23378.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23378.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23379.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23379.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42007.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42007.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42007.2	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42008.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42008.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42008.2	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_061.nt.1	78508.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_061.nt.1	78508.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_061.nt.2	78508.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_061.nt.2	78508.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_061.nt.3	78508.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_061.nt.3	78508.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_061.nt.4	78508.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_061.nt.4	78508.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_061.nt.5	78508.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_061.nt.5	78508.1	0.0	0.0	0.0	0.0	0.0	0.0

COLON CANCER CHIPS

For colon cancer two different chip designs were evaluated with overlapping sets of a total of 38 samples, comparing the expression patterns of colon cancer derived polyA+ RNA to polyA+ RNA isolated from a pool of 7 normal colon tissues. For the Colon Array Chip all 38 samples (23 Ascending colon carcinomas and 15 Rectosigmoidal carcinomas including: 5 stage I cancers, 15 stage II cancers, 15 stage III and 2 stage IV cancers, as well as 28 Grade1/2 and 10 Grade 3 cancers) were analyzed. The histopathologic grades for cancer are classified as follows: GX, cannot be assessed; G1, well differentiated; G2, Moderately differentiated; G3, poorly differentiated; and G4, undifferentiated. AJCC Cancer Staging Handbook, 5th Edition, 1998, page 9. For the Colon Array Chip analysis, samples were further divided into groups based on the

expression pattern of the known colon cancer associated gene Thymidilate Synthase (TS) (13 TS up 25 TS not up). The association of TS with advanced colorectal cancer is well documented. Paradiso *et al.*, *Br J Cancer* 82(3):560-7 (2000); Etienne *et al.*, *J Clin Oncol.* 20(12):2832-43 (2002); Aschele *et al. Clin Cancer Res.* 6(12):4797-802 (2000). For the Multi-Cancer Array Chip a subset of 27 of these samples (14 Ascending colon carcinomas and 13 Rectosigmoidal carcinomas including: 3 stage I cancers, 9 stage II cancers, 13 stage III and 2 stage IV cancers) were assessed.

The results for the statistically significant up-regulated genes on the Colon Array Chip are shown in Tables 6 and 7. The results for the statistically significant up-regulated genes on the Multi-Cancer Array Chip are shown in Table 8.

The first two columns of each table contain information about the sequence itself (Seq ID, Oligo Name), the next columns show the results obtained for all ("ALL") the colon samples, ascending colon carcinomas ("ASC"), Rectosigmoidal carcinomas ("RS"), cancers corresponding to stages I and II ("ST1,2"), stages III and IV ("ST3,4"), grades 1 and 2 ("GR1,2"), grade 3 ("GR3"), cancers exhibiting up-regulation of the TS gene ("TSup") or those not exhibiting up-regulation of the TS gene ("NOT TSup"). '%up' indicates the percentage of all experiments in which up-regulation of at least 2-fold was observed n=38 for the Colon Array Chip (n=27 for the Multi-Cancer Array Chip), '%valid up' indicates the percentage of experiments with valid expression values in which up-regulation of at least 2-fold was observed.

Table 6.

DEX ID	Oligo Name	Cln ALL %up n=38	Cln ALL % valid up n=38	Cln ASC %up n=23	Cln ASC % valid up n=23	Cln RS %up n=15	Cln RS % valid up n=15	Cln ST1, 2 %up n=20	Cln ST1,2 % valid up n=20	Cln ST3,4 %up n=18	Cln ST3,4 % valid up n=18
DEX0455_010.nt.1	37415.0	52.6	52.6	69.6	69.6	26.7	26.7	50.0	50.0	55.6	55.6
DEX0455_011.nt.1	35317.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_012.nt.1	34334.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_012.nt.1	34335.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_012.nt.1	34343.0	5.3	5.7	4.3	4.5	6.7	7.7	0.0	0.0	11.1	12.5
DEX0455_012.nt.1	34368.0	7.9	7.9	8.7	8.7	6.7	6.7	5.0	5.0	11.1	11.1
DEX0455_012.nt.1	34369.0	7.9	7.9	8.7	8.7	6.7	6.7	5.0	5.0	11.1	11.1
DEX0455_012.nt.2	34334.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

DEX0455_012.nt.2	34335.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_012.nt.2	34343.0	5.3	5.7	4.3	4.5	6.7	7.7	0.0	0.0	11.1	12.5
DEX0455_012.nt.2	34368.0	7.9	7.9	8.7	8.7	6.7	6.7	5.0	5.0	11.1	11.1
DEX0455_012.nt.2	34369.0	7.9	7.9	8.7	8.7	6.7	6.7	5.0	5.0	11.1	11.1
DEX0455_017.nt.1	21032.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_024.nt.1	17957.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0455_028.nt.1	30821.0	2.6	2.6	0.0	0.0	6.7	6.7	5.0	5.0	0.0	0.0
DEX0455_028.nt.1	41120.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_029.nt.1	30820.0	2.6	2.6	0.0	0.0	6.7	6.7	5.0	5.0	0.0	0.0
DEX0455_029.nt.1	30821.0	2.6	2.6	0.0	0.0	6.7	6.7	5.0	5.0	0.0	0.0
DEX0455_029.nt.1	30824.0	7.9	7.9	8.7	8.7	6.7	6.7	10.0	10.0	5.6	5.6
DEX0455_029.nt.1	30869.0	18.4	18.4	17.4	17.4	20.0	20.0	15.0	15.0	22.2	22.2
DEX0455_029.nt.1	41117.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_029.nt.1	41120.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_029.nt.1	41151.0	10.5	10.5	13.0	13.0	6.7	6.7	15.0	15.0	5.6	5.6
DEX0455_029.nt.1	41152.0	2.6	2.6	0.0	0.0	6.7	6.7	5.0	5.0	0.0	0.0
DEX0455_029.nt.2	30820.0	2.6	2.6	0.0	0.0	6.7	6.7	5.0	5.0	0.0	0.0
DEX0455_029.nt.2	30821.0	2.6	2.6	0.0	0.0	6.7	6.7	5.0	5.0	0.0	0.0
DEX0455_029.nt.2	30824.0	7.9	7.9	8.7	8.7	6.7	6.7	10.0	10.0	5.6	5.6
DEX0455_029.nt.2	30922.0	10.5	10.5	13.0	13.0	6.7	6.7	15.0	15.0	5.6	5.6
DEX0455_029.nt.2	41117.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_029.nt.2	41120.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_029.nt.2	41151.0	10.5	10.5	13.0	13.0	6.7	6.7	15.0	15.0	5.6	5.6
DEX0455_029.nt.2	41152.0	2.6	2.6	0.0	0.0	6.7	6.7	5.0	5.0	0.0	0.0
DEX0455_034.nt.1	16423.0	2.6	3.1	0.0	0.0	6.7	9.1	0.0	0.0	5.6	6.2
DEX0455_049.nt.1	36902.0	2.6	2.6	4.3	4.3	0.0	0.0	0.0	0.0	5.6	5.6
DEX0455_049.nt.2	36901.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0455_049.nt.2	36902.0	2.6	2.6	4.3	4.3	0.0	0.0	0.0	0.0	5.6	5.6
DEX0455_049.nt.3	36901.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1

DEX0455_049.nt.3	36902.0	2.6	2.6	4.3	4.3	0.0	0.0	0.0	0.0	5.6	5.6
DEX0455_049.nt.4	36901.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0455_049.nt.4	36902.0	2.6	2.6	4.3	4.3	0.0	0.0	0.0	0.0	5.6	5.6
DEX0455_049.nt.5	36901.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0455_049.nt.5	36902.0	2.6	2.6	4.3	4.3	0.0	0.0	0.0	0.0	5.6	5.6
DEX0455_050.nt.1	23378.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23378.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23379.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23379.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_061.nt.1	19803.0	2.6	2.6	4.3	4.3	0.0	0.0	0.0	0.0	5.6	5.6
DEX0455_061.nt.1	19804.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0455_061.nt.2	19803.0	2.6	2.6	4.3	4.3	0.0	0.0	0.0	0.0	5.6	5.6
DEX0455_061.nt.2	19804.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0455_061.nt.3	19803.0	2.6	2.6	4.3	4.3	0.0	0.0	0.0	0.0	5.6	5.6
DEX0455_061.nt.3	19804.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0455_061.nt.4	19803.0	2.6	2.6	4.3	4.3	0.0	0.0	0.0	0.0	5.6	5.6
DEX0455_061.nt.4	19804.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1
DEX0455_061.nt.5	19803.0	2.6	2.6	4.3	4.3	0.0	0.0	0.0	0.0	5.6	5.6
DEX0455_061.nt.5	19804.0	5.3	5.3	4.3	4.3	6.7	6.7	0.0	0.0	11.1	11.1

Table 7.

DEX ID	Oligo Name	Cln GR1,2 %up n=28	Cln GR1,2 %valid up n=28	Cln GR3 %up n=10	Cln GR3 %valid up n=10	Cln TS up %up n=13	Cln TS up %valid up n=13	Cln NOT TS up %up n=25	Cln NOT TS up %valid up n=25
DEX0455_010.nt.1	37415.0	46.4	46.4	70.0	70.0	46.2	46.2	56.0	56.0
DEX0455_011.nt.1	35317.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_012.nt.1	34334.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_012.nt.1	34335.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_012.nt.1	34343.0	3.6	3.7	10.0	12.5	15.4	15.4	0.0	0.0
DEX0455_012.nt.1	34368.0	7.1	7.1	10.0	10.0	15.4	15.4	4.0	4.0
DEX0455_012.nt.1	34369.0	7.1	7.1	10.0	10.0	15.4	15.4	4.0	4.0
DEX0455_012.nt.2	34334.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_012.nt.2	34335.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_012.nt.2	34343.0	3.6	3.7	10.0	12.5	15.4	15.4	0.0	0.0
DEX0455_012.nt.2	34368.0	7.1	7.1	10.0	10.0	15.4	15.4	4.0	4.0
DEX0455_012.nt.2	34369.0	7.1	7.1	10.0	10.0	15.4	15.4	4.0	4.0

DEX0455_017.nt.1	21032.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_024.nt.1	17957.0	7.1	7.1	0.0	0.0	7.7	7.7	4.0	4.0
DEX0455_028.nt.1	30821.0	3.6	3.6	0.0	0.0	7.7	7.7	0.0	0.0
DEX0455_028.nt.1	41120.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_029.nt.1	30820.0	3.6	3.6	0.0	0.0	7.7	7.7	0.0	0.0
DEX0455_029.nt.1	30821.0	3.6	3.6	0.0	0.0	7.7	7.7	0.0	0.0
DEX0455_029.nt.1	30824.0	10.7	10.7	0.0	0.0	15.4	15.4	4.0	4.0
DEX0455_029.nt.1	30869.0	17.9	17.9	20.0	20.0	30.8	30.8	12.0	12.0
DEX0455_029.nt.1	41117.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_029.nt.1	41120.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_029.nt.1	41151.0	14.3	14.3	0.0	0.0	15.4	15.4	8.0	8.0
DEX0455_029.nt.1	41152.0	3.6	3.6	0.0	0.0	7.7	7.7	0.0	0.0
DEX0455_029.nt.2	30820.0	3.6	3.6	0.0	0.0	7.7	7.7	0.0	0.0
DEX0455_029.nt.2	30821.0	3.6	3.6	0.0	0.0	7.7	7.7	0.0	0.0
DEX0455_029.nt.2	30824.0	10.7	10.7	0.0	0.0	15.4	15.4	4.0	4.0
DEX0455_029.nt.2	30922.0	14.3	14.3	0.0	0.0	15.4	15.4	8.0	8.0
DEX0455_029.nt.2	41117.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_029.nt.2	41120.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_029.nt.2	41151.0	14.3	14.3	0.0	0.0	15.4	15.4	8.0	8.0
DEX0455_029.nt.2	41152.0	3.6	3.6	0.0	0.0	7.7	7.7	0.0	0.0
DEX0455_034.nt.1	16423.0	0.0	0.0	10.0	12.5	7.7	8.3	0.0	0.0
DEX0455_049.nt.1	36902.0	3.6	3.6	0.0	0.0	7.7	7.7	0.0	0.0
DEX0455_049.nt.2	36901.0	3.6	3.6	10.0	10.0	15.4	15.4	0.0	0.0
DEX0455_049.nt.2	36902.0	3.6	3.6	0.0	0.0	7.7	7.7	0.0	0.0
DEX0455_049.nt.3	36901.0	3.6	3.6	10.0	10.0	15.4	15.4	0.0	0.0
DEX0455_049.nt.3	36902.0	3.6	3.6	0.0	0.0	7.7	7.7	0.0	0.0
DEX0455_049.nt.4	36901.0	3.6	3.6	10.0	10.0	15.4	15.4	0.0	0.0
DEX0455_049.nt.4	36902.0	3.6	3.6	0.0	0.0	7.7	7.7	0.0	0.0
DEX0455_049.nt.5	36901.0	3.6	3.6	10.0	10.0	15.4	15.4	0.0	0.0
DEX0455_049.nt.5	36902.0	3.6	3.6	0.0	0.0	7.7	7.7	0.0	0.0
DEX0455_050.nt.1	23378.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23378.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23379.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23379.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_061.nt.1	19803.0	0.0	0.0	10.0	10.0	0.0	0.0	4.0	4.0
DEX0455_061.nt.1	19804.0	0.0	0.0	20.0	20.0	7.7	7.7	4.0	4.0
DEX0455_061.nt.2	19803.0	0.0	0.0	10.0	10.0	0.0	0.0	4.0	4.0
DEX0455_061.nt.2	19804.0	0.0	0.0	20.0	20.0	7.7	7.7	4.0	4.0
DEX0455_061.nt.3	19803.0	0.0	0.0	10.0	10.0	0.0	0.0	4.0	4.0
DEX0455_061.nt.3	19804.0	0.0	0.0	20.0	20.0	7.7	7.7	4.0	4.0
DEX0455_061.nt.4	19803.0	0.0	0.0	10.0	10.0	0.0	0.0	4.0	4.0
DEX0455_061.nt.4	19804.0	0.0	0.0	20.0	20.0	7.7	7.7	4.0	4.0
DEX0455_061.nt.5	19803.0	0.0	0.0	10.0	10.0	0.0	0.0	4.0	4.0
DEX0455_061.nt.5	19804.0	0.0	0.0	20.0	20.0	7.7	7.7	4.0	4.0

Table 8.

DEX ID	Oligo Name	Cln Multi-Cancer ALL %up n=27	Cln Multi-Cancer ALL %valid up n=27	Cln Multi-Cancer ASC %up n=14	Cln Multi-Cancer ASC %valid up n=14	Cln Multi-Cancer RS %up n=13	Cln Multi-Cancer RS %valid up n=13
DEX0455_002.nt.1	79699.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_002.nt.1	79700.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_002.nt.1	79700.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	96339.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	96339.1	7.4	33.3	14.3	66.7	0.0	0.0

DEX0455_004.nt.1	96340.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	96340.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105991.0	3.7	20.0	7.1	50.0	0.0	0.0
DEX0455_004.nt.1	105991.1	3.7	25.0	7.1	33.3	0.0	0.0
DEX0455_004.nt.1	105992.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105992.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105996.0	3.7	3.7	7.1	7.1	0.0	0.0
DEX0455_004.nt.1	105996.1	7.4	7.4	7.1	7.1	7.7	7.7
DEX0455_004.nt.2	96339.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	96339.1	7.4	33.3	14.3	66.7	0.0	0.0
DEX0455_004.nt.2	96340.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	96340.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105991.0	3.7	20.0	7.1	50.0	0.0	0.0
DEX0455_004.nt.2	105991.1	3.7	25.0	7.1	33.3	0.0	0.0
DEX0455_004.nt.2	105992.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105992.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105996.0	3.7	3.7	7.1	7.1	0.0	0.0
DEX0455_004.nt.2	105996.1	7.4	7.4	7.1	7.1	7.7	7.7
DEX0455_011.nt.1	35317.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_011.nt.1	35317.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_012.nt.1	34334.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_012.nt.1	34334.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_012.nt.1	34335.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_012.nt.1	34335.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_012.nt.2	34334.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_012.nt.2	34334.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_012.nt.2	34335.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_012.nt.2	34335.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_017.nt.1	36482.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_017.nt.1	36482.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_033.nt.1	2023.0	7.4	7.4	14.3	14.3	0.0	0.0
DEX0455_033.nt.1	5327.0	3.7	3.8	7.1	7.7	0.0	0.0
DEX0455_033.nt.1	5328.0	3.7	3.7	7.1	7.1	0.0	0.0
DEX0455_035.nt.1	78519.0	51.9	51.9	50.0	50.0	53.8	53.8
DEX0455_035.nt.1	78519.1	44.4	46.2	42.9	46.2	46.2	46.2
DEX0455_035.nt.1	78520.0	33.3	33.3	42.9	42.9	23.1	23.1
DEX0455_035.nt.1	78520.1	33.3	33.3	42.9	42.9	23.1	23.1
DEX0455_035.nt.2	78519.0	51.9	51.9	50.0	50.0	53.8	53.8
DEX0455_035.nt.2	78519.1	44.4	46.2	42.9	46.2	46.2	46.2
DEX0455_035.nt.2	78520.0	33.3	33.3	42.9	42.9	23.1	23.1
DEX0455_035.nt.2	78520.1	33.3	33.3	42.9	42.9	23.1	23.1
DEX0455_035.nt.3	78519.0	51.9	51.9	50.0	50.0	53.8	53.8
DEX0455_035.nt.3	78519.1	44.4	46.2	42.9	46.2	46.2	46.2
DEX0455_035.nt.3	78520.0	33.3	33.3	42.9	42.9	23.1	23.1
DEX0455_035.nt.3	78520.1	33.3	33.3	42.9	42.9	23.1	23.1
DEX0455_038.nt.1	23542.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	23542.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	23543.0	3.7	3.7	0.0	0.0	7.7	7.7
DEX0455_038.nt.1	23543.1	3.7	3.7	0.0	0.0	7.7	7.7
DEX0455_038.nt.2	23542.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	23542.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	23543.0	3.7	3.7	0.0	0.0	7.7	7.7
DEX0455_038.nt.2	23543.1	3.7	3.7	0.0	0.0	7.7	7.7
DEX0455_038.nt.3	23542.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.3	23542.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.3	23543.0	3.7	3.7	0.0	0.0	7.7	7.7
DEX0455_038.nt.3	23543.1	3.7	3.7	0.0	0.0	7.7	7.7

DEX0455_047.nt.1	96212.0	7.4	7.4	14.3	14.3	0.0	0.0
DEX0455_047.nt.1	96212.1	7.4	7.4	14.3	14.3	0.0	0.0
DEX0455_047.nt.1	105764.0	7.4	8.0	14.3	14.3	0.0	0.0
DEX0455_047.nt.1	105764.1	7.4	7.4	14.3	14.3	0.0	0.0
DEX0455_047.nt.1	105767.0	3.7	3.7	7.1	7.1	0.0	0.0
DEX0455_047.nt.1	105767.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	105768.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	105768.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	96212.0	7.4	7.4	14.3	14.3	0.0	0.0
DEX0455_047.nt.2	96212.1	7.4	7.4	14.3	14.3	0.0	0.0
DEX0455_047.nt.2	105764.0	7.4	8.0	14.3	14.3	0.0	0.0
DEX0455_047.nt.2	105764.1	7.4	7.4	14.3	14.3	0.0	0.0
DEX0455_047.nt.2	105767.0	3.7	3.7	7.1	7.1	0.0	0.0
DEX0455_047.nt.2	105767.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	105768.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	105768.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_048.nt.1	1168.0	3.7	3.7	0.0	0.0	7.7	7.7
DEX0455_048.nt.2	1175.0	3.7	4.0	7.1	7.7	0.0	0.0
DEX0455_050.nt.1	23378.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23378.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23379.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23379.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42007.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42007.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42007.2	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42008.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42008.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42008.2	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_061.nt.1	78508.0	7.4	7.4	7.1	7.1	7.7	7.7
DEX0455_061.nt.1	78508.1	7.4	7.4	7.1	7.1	7.7	7.7
DEX0455_061.nt.2	78508.0	7.4	7.4	7.1	7.1	7.7	7.7
DEX0455_061.nt.2	78508.1	7.4	7.4	7.1	7.1	7.7	7.7
DEX0455_061.nt.3	78508.0	7.4	7.4	7.1	7.1	7.7	7.7
DEX0455_061.nt.3	78508.1	7.4	7.4	7.1	7.1	7.7	7.7
DEX0455_061.nt.4	78508.0	7.4	7.4	7.1	7.1	7.7	7.7
DEX0455_061.nt.4	78508.1	7.4	7.4	7.1	7.1	7.7	7.7
DEX0455_061.nt.5	78508.0	7.4	7.4	7.1	7.1	7.7	7.7
DEX0455_061.nt.5	78508.1	7.4	7.4	7.1	7.1	7.7	7.7

LUNG CANCER CHIPS

For lung cancer two different chip designs were evaluated with overlapping sets of a total of 29 samples, comparing the expression patterns of lung cancer derived polyA+ RNA to polyA+ RNA isolated from a pool of 12 normal lung tissues. For the Lung Array Chip all 29 samples (15 squamous cell carcinomas and 14 adenocarcinomas including 14 stage I and 15 stage II/III cancers) were analyzed and for the Multi-Cancer Array Chip a subset of 22 of these samples (10 squamous cell carcinomas, 12 adenocarcinomas) were assessed.

The results for the statistically significant up-regulated genes on the Lung Array Chip are shown in Table 9. The results for the statistically significant up-regulated genes on the Multi-Cancer Array Chip are shown in Table 10. The first two columns of each

table contain information about the sequence itself (DEX ID, Oligo Name), the next columns show the results obtained for all ("ALL") lung cancer samples, squamous cell carcinomas ("SQ"), adenocarcinomas ("AD"), or cancers corresponding to stage I ("ST1"), or stages II and III ("ST2,3"). '%up' indicates the percentage of all experiments in which up-regulation of at least 2-fold was observed (n=29 for Lung Array Chip, n=22 for Multi-Cancer Array Chip), '%valid up' indicates the percentage of experiments with valid expression values in which up-regulation of at least 2-fold was observed.

Table 9.

DEX ID	Oligo Name	Lng ALL %up n=29	Lng ALL % valid up n=29	Lng SQ %up n=15	Lng SQ % valid up n=15	Lng AD %up n=14	Lng AD % valid up n=14	Lng ST1 %up n=14	Lng ST1 % valid up n=14	Lng ST2, 3 %up n=15	Lng ST2,3 % valid up n=15
DEX0455_010.nt.1	791.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_010.nt.1	2720.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_010.nt.1	2721.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_010.nt.2	791.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_010.nt.2	2720.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_010.nt.2	2721.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_032.nt.1	2688.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_032.nt.1	2689.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_032.nt.1	5313.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_033.nt.1	2006.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_033.nt.1	2007.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_033.nt.1	2022.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_033.nt.1	2032.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_042.nt.1	889.0	93.1	93.1	100.0	100.0	85.7	85.7	92.9	92.9	93.3	93.3
DEX0455_048.nt.1	1009.0	3.4	3.4	6.7	6.7	0.0	0.0	0.0	0.0	6.7	6.7
DEX0455_048.nt.1	1010.0	6.9	6.9	13.3	13.3	0.0	0.0	0.0	0.0	13.3	13.3
DEX0455_048.nt.1	1011.0	6.9	6.9	13.3	13.3	0.0	0.0	7.1	7.1	6.7	6.7
DEX0455_048.nt.1	1169.0	3.4	3.4	6.7	6.7	0.0	0.0	0.0	0.0	6.7	6.7
DEX0455_048.nt.2	1009.0	3.4	3.4	6.7	6.7	0.0	0.0	0.0	0.0	6.7	6.7

DEX0455_048.nt.2	1010.0	6.9	6.9	13.3	13.3	0.0	0.0	0.0	0.0	13.3	13.3
DEX0455_048.nt.2	1011.0	6.9	6.9	13.3	13.3	0.0	0.0	7.1	7.1	6.7	6.7
DEX0455_048.nt.2	1169.0	3.4	3.4	6.7	6.7	0.0	0.0	0.0	0.0	6.7	6.7
DEX0455_048.nt.2	1174.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	7815.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23378.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23378.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42007.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42008.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_056.nt.1	1582.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_056.nt.1	1583.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_056.nt.1	2661.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_056.nt.1	3143.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_056.nt.1	3160.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_056.nt.1	3161.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_056.nt.1	3164.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_056.nt.1	3165.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_056.nt.2	1582.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_056.nt.2	1583.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_056.nt.2	2661.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_056.nt.2	3160.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_056.nt.2	3161.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_056.nt.2	3164.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_056.nt.2	3165.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_057.nt.1	7612.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_057.nt.1	7613.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_057.nt.2	7612.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_057.nt.2	7613.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Table 10.

DEX ID	Oligo Name	Lng Multi-Cancer ALL %up n=22	Lng Multi-Cancer ALL %valid up n=22	Lng Multi-Cancer SQ %up n=10	Lng Multi-Cancer SQ %valid up n=10	Lng Multi-Cancer AD %up n=12	Lng Multi-Cancer AD %valid up n=12
DEX0455_002.nt.1	79699.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_002.nt.1	79700.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_002.nt.1	79700.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	96339.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	96339.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	96340.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	96340.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105991.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105991.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105992.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105992.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105996.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105996.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	96339.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	96339.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	96340.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	96340.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105991.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105991.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105992.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105992.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105996.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105996.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_011.nt.1	35317.0	9.1	13.3	0.0	0.0	16.7	18.2
DEX0455_011.nt.1	35317.1	9.1	13.3	0.0	0.0	16.7	18.2
DEX0455_012.nt.1	34334.0	13.6	13.6	10.0	10.0	16.7	16.7
DEX0455_012.nt.1	34334.1	13.6	13.6	10.0	10.0	16.7	16.7
DEX0455_012.nt.1	34335.0	13.6	13.6	10.0	10.0	16.7	16.7
DEX0455_012.nt.1	34335.1	13.6	13.6	10.0	10.0	16.7	16.7
DEX0455_012.nt.2	34334.0	13.6	13.6	10.0	10.0	16.7	16.7
DEX0455_012.nt.2	34334.1	13.6	13.6	10.0	10.0	16.7	16.7
DEX0455_012.nt.2	34335.0	13.6	13.6	10.0	10.0	16.7	16.7
DEX0455_012.nt.2	34335.1	13.6	13.6	10.0	10.0	16.7	16.7
DEX0455_017.nt.1	36482.0	4.5	4.5	0.0	0.0	8.3	8.3
DEX0455_017.nt.1	36482.1	4.5	4.5	0.0	0.0	8.3	8.3
DEX0455_033.nt.1	2023.0	4.5	4.5	10.0	10.0	0.0	0.0
DEX0455_033.nt.1	5327.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_033.nt.1	5328.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_035.nt.1	78519.0	50.0	50.0	40.0	40.0	58.3	58.3
DEX0455_035.nt.1	78519.1	50.0	50.0	40.0	40.0	58.3	58.3
DEX0455_035.nt.1	78520.0	40.9	40.9	30.0	30.0	50.0	50.0
DEX0455_035.nt.1	78520.1	45.5	45.5	40.0	40.0	50.0	50.0
DEX0455_035.nt.2	78519.0	50.0	50.0	40.0	40.0	58.3	58.3
DEX0455_035.nt.2	78519.1	50.0	50.0	40.0	40.0	58.3	58.3
DEX0455_035.nt.2	78520.0	40.9	40.9	30.0	30.0	50.0	50.0
DEX0455_035.nt.2	78520.1	45.5	45.5	40.0	40.0	50.0	50.0
DEX0455_035.nt.3	78519.0	50.0	50.0	40.0	40.0	58.3	58.3
DEX0455_035.nt.3	78519.1	50.0	50.0	40.0	40.0	58.3	58.3
DEX0455_035.nt.3	78520.0	40.9	40.9	30.0	30.0	50.0	50.0
DEX0455_035.nt.3	78520.1	45.5	45.5	40.0	40.0	50.0	50.0
DEX0455_038.nt.1	23542.0	4.5	4.5	0.0	0.0	8.3	8.3
DEX0455_038.nt.1	23542.1	9.1	9.1	0.0	0.0	16.7	16.7

DEX0455_038.nt.1	23543.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	23543.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	23542.0	4.5	4.5	0.0	0.0	8.3	8.3
DEX0455_038.nt.2	23542.1	9.1	9.1	0.0	0.0	16.7	16.7
DEX0455_038.nt.2	23543.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	23543.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.3	23542.0	4.5	4.5	0.0	0.0	8.3	8.3
DEX0455_038.nt.3	23542.1	9.1	9.1	0.0	0.0	16.7	16.7
DEX0455_038.nt.3	23543.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.3	23543.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	96212.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	96212.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	105764.0	4.5	5.0	10.0	12.5	0.0	0.0
DEX0455_047.nt.1	105764.1	4.5	5.0	10.0	11.1	0.0	0.0
DEX0455_047.nt.1	105767.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	105767.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	105768.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	105768.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	96212.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	96212.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	105764.0	4.5	5.0	10.0	12.5	0.0	0.0
DEX0455_047.nt.2	105764.1	4.5	5.0	10.0	11.1	0.0	0.0
DEX0455_047.nt.2	105767.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	105767.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	105768.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	105768.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_048.nt.1	1168.0	4.5	4.5	10.0	10.0	0.0	0.0
DEX0455_048.nt.2	1175.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23378.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23378.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23379.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23379.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42007.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42007.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42007.2	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42008.0	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42008.1	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42008.2	0.0	0.0	0.0	0.0	0.0	0.0
DEX0455_061.nt.1	78508.0	31.8	31.8	30.0	30.0	33.3	33.3
DEX0455_061.nt.1	78508.1	31.8	31.8	20.0	20.0	41.7	41.7
DEX0455_061.nt.2	78508.0	31.8	31.8	30.0	30.0	33.3	33.3
DEX0455_061.nt.2	78508.1	31.8	31.8	20.0	20.0	41.7	41.7
DEX0455_061.nt.3	78508.0	31.8	31.8	30.0	30.0	33.3	33.3
DEX0455_061.nt.3	78508.1	31.8	31.8	20.0	20.0	41.7	41.7
DEX0455_061.nt.4	78508.0	31.8	31.8	30.0	30.0	33.3	33.3
DEX0455_061.nt.4	78508.1	31.8	31.8	20.0	20.0	41.7	41.7
DEX0455_061.nt.5	78508.0	31.8	31.8	30.0	30.0	33.3	33.3
DEX0455_061.nt.5	78508.1	31.8	31.8	20.0	20.0	41.7	41.7

PROSTATE CANCER

For prostate cancer three different chip designs were evaluated with overlapping sets of a total of 29 samples, comparing the expression patterns of prostate cancer or benign disease derived total RNA to total RNA isolated from a pool of 35 normal prostate tissues. For the Prostate1 Array and Prostate2 Array Chips all 29 samples (17 prostate

cancer samples, 12 non-malignant disease samples) were analyzed. For the Multi-Cancer Array Chip a subset of 28 of these samples (16 prostate cancer samples, 12 non-malignant disease samples) were analyzed.

The results for the statistically significant up-regulated genes on the Prostate1 Array Chip and the Prostate2 Array Chip are shown in Table 11. The results for the statistically significant up-regulated genes on the Multi-Cancer Array Chip are shown in Table 12. The first two columns of each table contain information about the sequence itself (DEX ID, Oligo Name), the next columns show the results obtained for prostate cancer samples ("CAN") or non-malignant disease samples ("DIS"). '%up' indicates the percentage of all experiments in which up-regulation of at least 2-fold was observed (n=29 for the Prostate2 Array Chip and the Multi-Cancer Array Chip), '%valid up' indicates the percentage of experiments with valid expression values in which up-regulation of at least 2-fold was observed.

Table 11.

DEX ID	Oligo Name	Pro CAN %up n=17	Pro CAN %valid up n=17	Pro DIS %up n=12	Pro DIS %valid up n=12
DEX0455_010.nt.1	28129.01	0.0	0.0	0.0	0.0
DEX0455_010.nt.1	28129.02	0.0	0.0	8.3	8.3
DEX0455_010.nt.2	28129.01	0.0	0.0	0.0	0.0
DEX0455_010.nt.2	28129.02	0.0	0.0	8.3	8.3
DEX0455_023.nt.1	8770.01	0.0	0.0	0.0	0.0
DEX0455_023.nt.1	8770.02	0.0	0.0	0.0	0.0
DEX0455_023.nt.1	8770.03	0.0	0.0	0.0	0.0
DEX0455_034.nt.1	26867.01	0.0	0.0	0.0	0.0
DEX0455_034.nt.1	26867.02	0.0	0.0	0.0	0.0
DEX0455_034.nt.1	32554.01	0.0	0.0	0.0	0.0
DEX0455_034.nt.1	32554.02	5.9	5.9	8.3	8.3
DEX0455_034.nt.1	32554.03	5.9	7.1	0.0	0.0
DEX0455_034.nt.1	32558.01	0.0	0.0	0.0	0.0
DEX0455_034.nt.1	32558.02	0.0	0.0	0.0	0.0
DEX0455_034.nt.1	32558.03	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	23492.01	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	23492.02	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	23542.01	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	23542.02	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	23546.01	5.9	33.3	0.0	0.0
DEX0455_038.nt.1	23546.02	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	24418.01	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	24418.02	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	24422.01	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	24422.02	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	27965.01	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	27965.02	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	28535.01	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	28535.02	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	23492.01	0.0	0.0	0.0	0.0

DEX0455_038.nt.2	23492.02	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	23542.01	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	23542.02	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	23684.01	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	23684.02	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	24418.01	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	24418.02	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	27965.01	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	27965.02	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	28535.01	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	28535.02	0.0	0.0	0.0	0.0
DEX0455_038.nt.3	23492.01	0.0	0.0	0.0	0.0
DEX0455_038.nt.3	23492.02	0.0	0.0	0.0	0.0
DEX0455_038.nt.3	23542.01	0.0	0.0	0.0	0.0
DEX0455_038.nt.3	23542.02	0.0	0.0	0.0	0.0
DEX0455_038.nt.3	27965.01	0.0	0.0	0.0	0.0
DEX0455_038.nt.3	27965.02	0.0	0.0	0.0	0.0
DEX0455_038.nt.3	28535.01	0.0	0.0	0.0	0.0
DEX0455_038.nt.3	28535.02	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23378.01	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23378.02	5.9	11.1	0.0	0.0
DEX0455_057.nt.1	33332.01	0.0	0.0	0.0	0.0
DEX0455_057.nt.1	33332.02	0.0	0.0	0.0	0.0
DEX0455_057.nt.2	33332.01	0.0	0.0	0.0	0.0
DEX0455_057.nt.2	33332.02	0.0	0.0	0.0	0.0

Table 12.

DEX ID	Oligo Name	Pro Multi-Cancer CAN %up n=16	Pro Multi-Cancer CAN %valid up n=16	Pro Multi-Cancer DIS %up n=12	Pro Multi-Cancer DIS %valid up n=12
DEX0455_002.nt.1	79699.1	0.0	0.0	0.0	0.0
DEX0455_002.nt.1	79700.0	0.0	0.0	0.0	0.0
DEX0455_002.nt.1	79700.1	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	96339.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	96339.1	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	96340.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	96340.1	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105991.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105991.1	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105992.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105992.1	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105996.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.1	105996.1	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	96339.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	96339.1	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	96340.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	96340.1	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105991.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105991.1	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105992.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105992.1	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105996.0	0.0	0.0	0.0	0.0
DEX0455_004.nt.2	105996.1	0.0	0.0	0.0	0.0
DEX0455_011.nt.1	35317.0	0.0	0.0	0.0	0.0
DEX0455_011.nt.1	35317.1	0.0	0.0	0.0	0.0
DEX0455_012.nt.1	34334.0	17.6	18.8	0.0	0.0

DEX0455_012.nt.1	34334.1	23.5	25.0	0.0	0.0
DEX0455_012.nt.1	34335.0	23.5	26.7	8.3	8.3
DEX0455_012.nt.1	34335.1	17.6	18.8	0.0	0.0
DEX0455_012.nt.2	34334.0	17.6	18.8	0.0	0.0
DEX0455_012.nt.2	34334.1	23.5	25.0	0.0	0.0
DEX0455_012.nt.2	34335.0	23.5	26.7	8.3	8.3
DEX0455_012.nt.2	34335.1	17.6	18.8	0.0	0.0
DEX0455_017.nt.1	36482.0	5.9	6.7	0.0	0.0
DEX0455_017.nt.1	36482.1	5.9	6.2	0.0	0.0
DEX0455_033.nt.1	2023.0	0.0	0.0	0.0	0.0
DEX0455_033.nt.1	5327.0	0.0	0.0	0.0	0.0
DEX0455_033.nt.1	5328.0	0.0	0.0	0.0	0.0
DEX0455_035.nt.1	78519.0	0.0	0.0	0.0	0.0
DEX0455_035.nt.1	78519.1	0.0	0.0	0.0	0.0
DEX0455_035.nt.1	78520.0	0.0	0.0	0.0	0.0
DEX0455_035.nt.1	78520.1	0.0	0.0	0.0	0.0
DEX0455_035.nt.2	78519.0	0.0	0.0	0.0	0.0
DEX0455_035.nt.2	78519.1	0.0	0.0	0.0	0.0
DEX0455_035.nt.2	78520.0	0.0	0.0	0.0	0.0
DEX0455_035.nt.2	78520.1	0.0	0.0	0.0	0.0
DEX0455_035.nt.3	78519.0	0.0	0.0	0.0	0.0
DEX0455_035.nt.3	78519.1	0.0	0.0	0.0	0.0
DEX0455_035.nt.3	78520.0	0.0	0.0	0.0	0.0
DEX0455_035.nt.3	78520.1	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	23542.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	23542.1	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	23543.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.1	23543.1	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	23542.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	23542.1	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	23543.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.2	23543.1	0.0	0.0	0.0	0.0
DEX0455_038.nt.3	23542.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.3	23542.1	0.0	0.0	0.0	0.0
DEX0455_038.nt.3	23543.0	0.0	0.0	0.0	0.0
DEX0455_038.nt.3	23543.1	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	96212.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	96212.1	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	105764.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	105764.1	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	105767.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	105767.1	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	105768.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.1	105768.1	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	96212.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	96212.1	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	105764.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	105764.1	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	105767.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	105767.1	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	105768.0	0.0	0.0	0.0	0.0
DEX0455_047.nt.2	105768.1	0.0	0.0	0.0	0.0
DEX0455_048.nt.1	1168.0	0.0	0.0	8.3	8.3
DEX0455_048.nt.2	1175.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23378.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23378.1	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	23379.0	0.0	0.0	0.0	0.0

DEX0455_050.nt.1	23379.1	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42007.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42007.1	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42007.2	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42008.0	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42008.1	0.0	0.0	0.0	0.0
DEX0455_050.nt.1	42008.2	0.0	0.0	0.0	0.0
DEX0455_061.nt.1	78508.0	0.0	0.0	0.0	0.0
DEX0455_061.nt.1	78508.1	0.0	0.0	0.0	0.0
DEX0455_061.nt.2	78508.0	0.0	0.0	0.0	0.0
DEX0455_061.nt.2	78508.1	0.0	0.0	0.0	0.0
DEX0455_061.nt.3	78508.0	0.0	0.0	0.0	0.0
DEX0455_061.nt.3	78508.1	0.0	0.0	0.0	0.0
DEX0455_061.nt.4	78508.0	0.0	0.0	0.0	0.0
DEX0455_061.nt.4	78508.1	0.0	0.0	0.0	0.0
DEX0455_061.nt.5	78508.0	0.0	0.0	0.0	0.0
DEX0455_061.nt.5	78508.1	0.0	0.0	0.0	0.0

SEQ ID NO: 1-128 was up-regulated on various tissue microarrays. Accordingly, nucleotide SEQ ID NO: 1-128 or the encoded protein SEQ ID NO: 129-295 may be used as a cancer therapeutic and/or diagnostic target for the tissues in which expression is shown.

The following table lists the location (Oligo Location) where the microarray oligos (Oligo ID) map on the transcripts (DEX ID) of the present invention. Each Oligo ID may have been printed multiple times on a single chip as replicates. The Oligo Name is an exemplary replicate (e.g. 1000.01) for the Oligo ID (e.g. 1000), and data from other replicates (e.g. 1000.02, 1000.03) may be reported. Additionally, the Array (Chip Name) that each oligo and oligo replicates were printed on is included.

DEX NT ID	Oligo ID	Oligo Name	Chip Name	Oligo Location
DEX0455_001.nt.1	34930	34930.01	Ovarian array	4736-4795
DEX0455_002.nt.1	21577	21577.02	Ovarian array	198-257
DEX0455_002.nt.1	79699	79699.0	Multi-Cancer array	1430-1489
DEX0455_002.nt.1	21553	21553.01	Ovarian array	513-572
DEX0455_002.nt.1	79700	79700.0	Multi-Cancer array	1429-1488
DEX0455_003.nt.1	17466	17466.02	Ovarian array	1075-1134
DEX0455_004.nt.1	96340	96340.0	Multi-Cancer array	6807-6866
DEX0455_004.nt.1	96339	96339.0	Multi-Cancer array	6906-6965
DEX0455_004.nt.1	105991	105991.0	Multi-Cancer array	6906-6965
DEX0455_004.nt.1	105992	105992.0	Multi-Cancer array	6807-6866
DEX0455_004.nt.1	105996	105996.0	Multi-Cancer array	8462-8521
DEX0455_004.nt.2	96340	96340.0	Multi-Cancer array	5651-5710
DEX0455_004.nt.2	105991	105991.0	Multi-Cancer array	5750-5809
DEX0455_004.nt.2	105992	105992.0	Multi-Cancer array	5651-5710
DEX0455_004.nt.2	105996	105996.0	Multi-Cancer array	7306-7365

DEX0455_004.nt.2	96339	96339.0	Multi-Cancer array	5750-5809
DEX0455_005.nt.1	24874	24874.01	Ovarian array	475-534
DEX0455_005.nt.1	20619	20619.02	Ovarian array	472-531
DEX0455_005.nt.2	24874	24874.01	Ovarian array	475-534
DEX0455_007.nt.1	30109	30109.01	Ovarian array	982-1041
DEX0455_008.nt.1	22387	22387.01	Ovarian array	1666-1725
DEX0455_008.nt.1	18508	18508.02	Ovarian array	1193-1252
DEX0455_009.nt.1	9720	9720.02	Ovarian array	1745-1804
DEX0455_010.nt.1	2721	2721.0	Lung array	501-560
DEX0455_010.nt.1	37415	37415.0	Colon array	1040-1099
DEX0455_010.nt.1	32151	32151.0	Breast array	748-807
DEX0455_010.nt.1	2720	2720.0	Lung array	542-601
DEX0455_010.nt.1	21675	21675.02	Ovarian array	965-1024
DEX0455_010.nt.1	20627	20627.02	Ovarian array	250-309
DEX0455_010.nt.1	28129	28129.02	Prostate1 array	964-1023
DEX0455_010.nt.1	791	791.0	Lung array	1045-1104
DEX0455_010.nt.2	2720	2720.0	Lung array	379-438
DEX0455_010.nt.2	32151	32151.0	Breast array	585-644
DEX0455_010.nt.2	28129	28129.02	Prostate1 array	801-860
DEX0455_010.nt.2	37415	37415.0	Colon array	877-936
DEX0455_010.nt.2	21675	21675.02	Ovarian array	802-861
DEX0455_010.nt.2	791	791.0	Lung array	882-941
DEX0455_010.nt.2	2721	2721.0	Lung array	338-397
DEX0455_011.nt.1	35317	35317.0	Colon array	398-457
DEX0455_012.nt.1	34368	34368.0	Colon array	2484-2543
DEX0455_012.nt.1	34369	34369.0	Colon array	2441-2500
DEX0455_012.nt.1	34334	34334.0	Colon array	3108-3167
DEX0455_012.nt.1	34343	34343.0	Colon array	472-531
DEX0455_012.nt.1	34335	34335.0	Colon array	3022-3081
DEX0455_012.nt.2	34334	34334.0	Colon array	2527-2586
DEX0455_012.nt.2	34343	34343.0	Colon array	472-531
DEX0455_012.nt.2	34369	34369.0	Colon array	1860-1919
DEX0455_012.nt.2	34335	34335.0	Colon array	2441-2500
DEX0455_012.nt.2	34368	34368.0	Colon array	1903-1962
DEX0455_013.nt.1	9838	9838.02	Ovarian array	1304-1363
DEX0455_014.nt.1	10624	10624.02	Ovarian array	1832-1891
DEX0455_014.nt.1	14604	14604.01	Ovarian array	925-984
DEX0455_015.nt.1	19518	19518.01	Ovarian array	277-336
DEX0455_016.nt.1	23734	23734.02	Ovarian array	531-590
DEX0455_017.nt.1	28221	28221.0	Breast array	679-738
DEX0455_017.nt.1	21032	21032.0	Colon array	314-373
DEX0455_017.nt.1	36482	36482.0	Multi-Cancer array	314-373
DEX0455_018.nt.1	21575	21575.01	Ovarian array	1516-1575
DEX0455_018.nt.1	21571	21571.02	Ovarian array	623-682
DEX0455_018.nt.1	21609	21609.02	Ovarian array	933-992
DEX0455_018.nt.2	21575	21575.01	Ovarian array	2287-2346
DEX0455_019.nt.1	20669	20669.01	Ovarian array	615-674

DEX0455_021.nt.1	23780	23780.01	Ovarian array	517-576
DEX0455_021.nt.1	21469	21469.02	Ovarian array	430-489
DEX0455_021.nt.1	21433	21433.01	Ovarian array	518-577
DEX0455_021.nt.1	21475	21475.01	Ovarian array	517-576
DEX0455_021.nt.2	21469	21469.02	Ovarian array	1528-1587
DEX0455_021.nt.2	21475	21475.01	Ovarian array	1615-1674
DEX0455_021.nt.2	21433	21433.01	Ovarian array	1616-1675
DEX0455_021.nt.2	23780	23780.01	Ovarian array	1615-1674
DEX0455_021.nt.3	21433	21433.01	Ovarian array	1859-1918
DEX0455_021.nt.3	21475	21475.01	Ovarian array	1858-1917
DEX0455_021.nt.3	21469	21469.02	Ovarian array	1771-1830
DEX0455_021.nt.3	23780	23780.01	Ovarian array	1858-1917
DEX0455_021.nt.4	21469	21469.02	Ovarian array	1914-1973
DEX0455_021.nt.4	21475	21475.01	Ovarian array	2001-2060
DEX0455_021.nt.4	21433	21433.01	Ovarian array	2002-2061
DEX0455_022.nt.1	9920	9920.02	Ovarian array	1022-1081
DEX0455_022.nt.1	20311	20311.01	Ovarian array	718-777
DEX0455_022.nt.1	20299	20299.01	Ovarian array	529-588
DEX0455_022.nt.1	23280	23280.0	Breast array	427-486
DEX0455_022.nt.1	20317	20317.02	Ovarian array	718-777
DEX0455_022.nt.2	9920	9920.02	Ovarian array	1016-1075
DEX0455_022.nt.2	20311	20311.01	Ovarian array	712-771
DEX0455_022.nt.2	20317	20317.02	Ovarian array	712-771
DEX0455_022.nt.2	20299	20299.01	Ovarian array	552-611
DEX0455_022.nt.3	9920	9920.02	Ovarian array	613-672
DEX0455_022.nt.3	20317	20317.02	Ovarian array	309-368
DEX0455_022.nt.3	20311	20311.01	Ovarian array	309-368
DEX0455_023.nt.1	16374	16374.02	Ovarian array	2119-2178
DEX0455_023.nt.1	8770	8770.03	Prostate2 array	1897-1956
DEX0455_023.nt.1	16378	16378.01	Ovarian array	937-996
DEX0455_023.nt.1	16187	16187.01	Ovarian array	666-725
DEX0455_024.nt.1	21507	21507.01	Ovarian array	2357-2416
DEX0455_024.nt.1	21487	21487.01	Ovarian array	796-855
DEX0455_024.nt.1	12149	12149.01	Ovarian array	2439-2498
DEX0455_024.nt.1	21547	21547.02	Ovarian array	1555-1614
DEX0455_024.nt.1	17957	17957.0	Colon array	2002-2061
DEX0455_024.nt.2	21507	21507.01	Ovarian array	1790-1849
DEX0455_024.nt.2	12149	12149.01	Ovarian array	1872-1931
DEX0455_024.nt.2	21547	21547.02	Ovarian array	988-1047
DEX0455_024.nt.2	17957	17957.0	Colon array	1435-1494
DEX0455_025.nt.1	12167	12167.01	Ovarian array	475-534
DEX0455_025.nt.1	16964	16964.02	Ovarian array	3509-3568
DEX0455_025.nt.1	16956	16956.02	Ovarian array	3533-3592
DEX0455_025.nt.1	16958	16958.01	Ovarian array	808-867
DEX0455_025.nt.1	19010	19010.01	Ovarian array	1260-1319
DEX0455_025.nt.2	12167	12167.01	Ovarian array	475-534
DEX0455_025.nt.2	16964	16964.02	Ovarian array	2465-2524

DEX0455_025.nt.2	16956	16956.02	Ovarian array	2489-2548
DEX0455_025.nt.2	16958	16958.01	Ovarian array	808-867
DEX0455_025.nt.2	19010	19010.01	Ovarian array	1260-1319
DEX0455_025.nt.3	12167	12167.01	Ovarian array	475-534
DEX0455_025.nt.3	19010	19010.01	Ovarian array	1260-1319
DEX0455_025.nt.3	16958	16958.01	Ovarian array	808-867
DEX0455_025.nt.4	19010	19010.01	Ovarian array	1260-1319
DEX0455_025.nt.4	16956	16956.02	Ovarian array	2167-2226
DEX0455_025.nt.4	16964	16964.02	Ovarian array	2143-2202
DEX0455_025.nt.4	12167	12167.01	Ovarian array	475-534
DEX0455_027.nt.1	21549	21549.01	Ovarian array	1483-1542
DEX0455_028.nt.1	41120	41120.0	Colon array	477-536
DEX0455_028.nt.1	30821	30821.0	Colon array	673-732
DEX0455_029.nt.1	41151	41151.0	Colon array	2429-2488
DEX0455_029.nt.1	22113	22113.01	Ovarian array	3222-3281
DEX0455_029.nt.1	30869	30869.0	Colon array	5572-5631
DEX0455_029.nt.1	41120	41120.0	Colon array	1984-2043
DEX0455_029.nt.1	23386	23386.01	Ovarian array	2429-2488
DEX0455_029.nt.1	30820	30820.0	Colon array	2388-2447
DEX0455_029.nt.1	41117	41117.0	Colon array	2296-2355
DEX0455_029.nt.1	30821	30821.0	Colon array	2348-2407
DEX0455_029.nt.1	23400	23400.02	Ovarian array	2296-2355
DEX0455_029.nt.1	41152	41152.0	Colon array	2372-2431
DEX0455_029.nt.1	17430	17430.02	Ovarian array	2388-2447
DEX0455_029.nt.1	30824	30824.0	Colon array	5798-5857
DEX0455_029.nt.1	17448	17448.01	Ovarian array	5798-5857
DEX0455_029.nt.2	41120	41120.0	Colon array	2412-2471
DEX0455_029.nt.2	17430	17430.02	Ovarian array	2816-2875
DEX0455_029.nt.2	23386	23386.01	Ovarian array	2857-2916
DEX0455_029.nt.2	30824	30824.0	Colon array	5101-5160
DEX0455_029.nt.2	17424	17424.01	Ovarian array	4880-4939
DEX0455_029.nt.2	30922	30922.0	Colon array	4880-4939
DEX0455_029.nt.2	23400	23400.02	Ovarian array	2724-2783
DEX0455_029.nt.2	41152	41152.0	Colon array	2800-2859
DEX0455_029.nt.2	30820	30820.0	Colon array	2816-2875
DEX0455_029.nt.2	22113	22113.01	Ovarian array	3650-3709
DEX0455_029.nt.2	41117	41117.0	Colon array	2724-2783
DEX0455_029.nt.2	41151	41151.0	Colon array	2857-2916
DEX0455_029.nt.2	30821	30821.0	Colon array	2776-2835
DEX0455_029.nt.2	17448	17448.01	Ovarian array	5101-5160
DEX0455_030.nt.1	17204	17204.02	Ovarian array	1225-1284
DEX0455_030.nt.1	17262	17262.02	Ovarian array	1011-1070
DEX0455_030.nt.1	17278	17278.02	Ovarian array	991-1050
DEX0455_030.nt.1	11613	11613.01	Ovarian array	1011-1070
DEX0455_030.nt.2	17274	17274.02	Ovarian array	696-755
DEX0455_030.nt.2	17204	17204.02	Ovarian array	984-1043
DEX0455_030.nt.2	17278	17278.02	Ovarian array	713-772

DEX0455_030.nt.2	17262	17262.02	Ovarian array	733-792
DEX0455_031.nt.1	20773	20773.02	Ovarian array	2724-2783
DEX0455_032.nt.1	2688	2688.0	Lung array	952-1011
DEX0455_032.nt.1	11585	11585.01	Ovarian array	1342-1401
DEX0455_032.nt.1	2689	2689.0	Lung array	910-969
DEX0455_032.nt.1	18556	18556.02	Ovarian array	952-1011
DEX0455_032.nt.1	5313	5313.0	Lung array	1342-1401
DEX0455_033.nt.1	5328	5328.0	Multi-Cancer array	402-461
DEX0455_033.nt.1	2006	2006.0	Lung array	402-461
DEX0455_033.nt.1	2022	2022.0	Lung array	482-541
DEX0455_033.nt.1	2032	2032.0	Lung array	290-349
DEX0455_033.nt.1	2007	2007.0	Lung array	361-420
DEX0455_033.nt.1	5327	5327.0	Multi-Cancer array	442-501
DEX0455_033.nt.1	2023	2023.0	Multi-Cancer array	442-501
DEX0455_034.nt.1	10722	10722.02	Ovarian array	2454-2513
DEX0455_034.nt.1	32554	32554.02	Prostate2 array	1815-1874
DEX0455_034.nt.1	21421	21421.02	Ovarian array	1815-1874
DEX0455_034.nt.1	32558	32558.01	Prostate2 array	1053-1112
DEX0455_034.nt.1	16423	16423.0	Colon array	885-944
DEX0455_034.nt.1	21401	21401.02	Ovarian array	1053-1112
DEX0455_034.nt.1	26867	26867.01	Prostate1 array	2454-2513
DEX0455_035.nt.1	78519	78519.0	Multi-Cancer array	923-982
DEX0455_035.nt.1	78520	78520.0	Multi-Cancer array	857-916
DEX0455_035.nt.1	103385	103385.01	Ovarian array	926-985
DEX0455_035.nt.2	78519	78519.0	Multi-Cancer array	1152-1211
DEX0455_035.nt.2	103385	103385.01	Ovarian array	1155-1214
DEX0455_035.nt.2	78520	78520.0	Multi-Cancer array	1086-1145
DEX0455_035.nt.3	103385	103385.01	Ovarian array	1034-1093
DEX0455_035.nt.3	78519	78519.0	Multi-Cancer array	1031-1090
DEX0455_035.nt.3	78520	78520.0	Multi-Cancer array	965-1024
DEX0455_035.nt.3	21144	21144.0	Breast array	126-185
DEX0455_035.nt.3	21143	21143.0	Breast array	212-271
DEX0455_036.nt.1	92327	92327.01	Ovarian array	177-236
DEX0455_037.nt.1	17490	17490.01	Ovarian array	894-953
DEX0455_037.nt.1	11575	11575.01	Ovarian array	892-951
DEX0455_037.nt.1	17486	17486.01	Ovarian array	887-946
DEX0455_037.nt.2	17490	17490.01	Ovarian array	1459-1518
DEX0455_037.nt.2	11575	11575.01	Ovarian array	1457-1516
DEX0455_037.nt.3	17490	17490.01	Ovarian array	2399-2458
DEX0455_037.nt.3	11575	11575.01	Ovarian array	2397-2456
DEX0455_037.nt.3	17486	17486.01	Ovarian array	2392-2451
DEX0455_037.nt.4	17490	17490.01	Ovarian array	515-574
DEX0455_037.nt.4	17486	17486.01	Ovarian array	508-567
DEX0455_037.nt.4	11575	11575.01	Ovarian array	513-572
DEX0455_037.nt.5	17486	17486.01	Ovarian array	571-630
DEX0455_037.nt.5	17490	17490.01	Ovarian array	578-637
DEX0455_037.nt.5	11575	11575.01	Ovarian array	576-635

DEX0455_038.nt.1	23543	23543.0	Multi-Cancer array	5011-5070
DEX0455_038.nt.1	23492	23492.02	Prostate1 array	5433-5492
DEX0455_038.nt.1	23546	23546.01	Prostate1 array	3874-3933
DEX0455_038.nt.1	24422	24422.01	Prostate1 array	3874-3933
DEX0455_038.nt.1	23542	23542.0	Multi-Cancer array	5118-5177
DEX0455_038.nt.1	24418	24418.01	Prostate1 array	2859-2918
DEX0455_038.nt.1	27965	27965.01	Prostate1 array	1956-2015
DEX0455_038.nt.1	28535	28535.01	Prostate1 array	5154-5213
DEX0455_038.nt.2	27965	27965.01	Prostate1 array	1956-2015
DEX0455_038.nt.2	23543	23543.0	Multi-Cancer array	4443-4502
DEX0455_038.nt.2	28535	28535.01	Prostate1 array	4586-4645
DEX0455_038.nt.2	23492	23492.02	Prostate1 array	4865-4924
DEX0455_038.nt.2	24418	24418.01	Prostate1 array	2859-2918
DEX0455_038.nt.2	23542	23542.0	Multi-Cancer array	4550-4609
DEX0455_038.nt.2	23684	23684.02	Prostate1 array	3719-3778
DEX0455_038.nt.3	23543	23543.0	Multi-Cancer array	2528-2587
DEX0455_038.nt.3	23492	23492.02	Prostate1 array	2950-3009
DEX0455_038.nt.3	23542	23542.0	Multi-Cancer array	2635-2694
DEX0455_038.nt.3	27965	27965.01	Prostate1 array	1693-1752
DEX0455_038.nt.3	28535	28535.01	Prostate1 array	2671-2730
DEX0455_039.nt.1	21505	21505.02	Ovarian array	355-414
DEX0455_039.nt.2	11527	11527.01	Ovarian array	467-526
DEX0455_040.nt.1	21489	21489.02	Ovarian array	281-340
DEX0455_040.nt.1	21501	21501.02	Ovarian array	772-831
DEX0455_040.nt.1	21511	21511.01	Ovarian array	586-645
DEX0455_040.nt.2	21489	21489.02	Ovarian array	698-757
DEX0455_040.nt.2	21511	21511.01	Ovarian array	1003-1062
DEX0455_040.nt.2	21501	21501.02	Ovarian array	1189-1248
DEX0455_041.nt.1	16980	16980.01	Ovarian array	125-184
DEX0455_041.nt.1	16998	16998.0	Breast array	125-184
DEX0455_041.nt.1	12155	12155.01	Ovarian array	309-368
DEX0455_042.nt.1	889	889.0	Lung array	346-405
DEX0455_042.nt.1	18214	18214.02	Ovarian array	346-405
DEX0455_043.nt.1	14656	14656.02	Ovarian array	463-522
DEX0455_045.nt.1	36013	36013.01	Ovarian array	382-441
DEX0455_046.nt.1	17314	17314.01	Ovarian array	614-673
DEX0455_046.nt.1	19072	19072.0	Breast array	614-673
DEX0455_047.nt.1	105768	105768.0	Multi-Cancer array	3274-3333
DEX0455_047.nt.1	96212	96212.0	Multi-Cancer array	2703-2762
DEX0455_047.nt.1	105767	105767.0	Multi-Cancer array	3314-3373
DEX0455_047.nt.1	105764	105764.0	Multi-Cancer array	2703-2762
DEX0455_047.nt.2	105768	105768.0	Multi-Cancer array	1478-1537
DEX0455_047.nt.2	105767	105767.0	Multi-Cancer array	1518-1577
DEX0455_047.nt.2	96212	96212.0	Multi-Cancer array	907-966
DEX0455_048.nt.1	1169	1169.0	Lung array	175-234
DEX0455_048.nt.1	1011	1011.0	Lung array	202-261
DEX0455_048.nt.1	1009	1009.0	Lung array	192-251

DEX0455_048.nt.1	1010	1010.0	Lung array	242-301
DEX0455_048.nt.1	1168	1169.0	Multi-Cancer array	180-239
DEX0455_048.nt.2	1169	1169.0	Lung array	386-445
DEX0455_048.nt.2	1011	1011.0	Lung array	413-472
DEX0455_048.nt.2	1009	1009.0	Lung array	403-462
DEX0455_048.nt.2	1175	1175.0	Multi-Cancer array	254-313
DEX0455_048.nt.2	1168	1168.0	Multi-Cancer array	391-450
DEX0455_048.nt.2	1174	1174.0	Lung array	259-318
DEX0455_048.nt.2	1010	1010.0	Lung array	453-512
DEX0455_049.nt.1	11511	11511.02	Ovarian array	2111-2170
DEX0455_049.nt.1	36902	36902.0	Colon array	928-987
DEX0455_049.nt.2	36901	36901.0	Colon array	621-680
DEX0455_049.nt.2	11511	11511.02	Ovarian array	1528-1587
DEX0455_049.nt.2	36902	36902.0	Colon array	582-641
DEX0455_049.nt.3	36901	36901.0	Colon array	967-1026
DEX0455_049.nt.4	11511	11511.02	Ovarian array	2102-2161
DEX0455_049.nt.4	36902	36902.0	Colon array	1156-1215
DEX0455_049.nt.4	36901	36901.0	Colon array	1195-1254
DEX0455_049.nt.5	36902	36902.0	Colon array	299-358
DEX0455_049.nt.5	11511	11511.02	Ovarian array	1245-1304
DEX0455_050.nt.1	29736	29736.0	Breast array	171-230
DEX0455_050.nt.1	7815	7815.0	Lung array	385-444
DEX0455_050.nt.1	23378	23378.0	Breast array	684-743
DEX0455_050.nt.1	42008	42008.0	Multi-Cancer array	329-388
DEX0455_050.nt.1	42007	42007.0	Multi-Cancer array	329-388
DEX0455_050.nt.1	22136	22136.0	Breast array	636-695
DEX0455_050.nt.1	23379	23379.0	Breast array	385-444
DEX0455_052.nt.1	91971	91971.01	Ovarian array	1686-1745
DEX0455_054.nt.1	19799	19799.0	Breast array	1918-1977
DEX0455_055.nt.1	20541	20541.01	Ovarian array	1705-1764
DEX0455_055.nt.1	12731	12731.0	Breast array	1601-1660
DEX0455_055.nt.1	12732	12732.0	Breast array	1395-1454
DEX0455_055.nt.1	11273	11273.02	Ovarian array	1815-1874
DEX0455_055.nt.2	20541	20541.01	Ovarian array	1403-1462
DEX0455_055.nt.2	12731	12731.0	Breast array	1299-1358
DEX0455_055.nt.2	12732	12732.0	Breast array	1136-1195
DEX0455_055.nt.2	11273	11273.02	Ovarian array	1513-1572
DEX0455_055.nt.3	12732	12732.0	Breast array	568-627
DEX0455_055.nt.3	12731	12731.0	Breast array	731-790
DEX0455_055.nt.3	20541	20541.01	Ovarian array	835-894
DEX0455_056.nt.1	23444	23444.01	Ovarian array	2588-2647
DEX0455_056.nt.1	3161	3161.0	Lung array	2547-2606
DEX0455_056.nt.1	3164	3164.0	Lung array	3317-3376
DEX0455_056.nt.1	3160	3160.0	Lung array	2588-2647
DEX0455_056.nt.1	3165	3165.0	Lung array	3277-3336
DEX0455_056.nt.1	1583	1583.0	Lung array	3277-3336
DEX0455_056.nt.1	18520	18520.02	Ovarian array	3317-3376

DEX0455_056.nt.1	3143	3143.0	Lung array	3107-3166
DEX0455_056.nt.1	1582	1582.0	Lung array	3317-3376
DEX0455_056.nt.1	22734	22734.02	Ovarian array	3317-3376
DEX0455_056.nt.1	2661	2661.0	Lung array	3523-3582
DEX0455_056.nt.2	23444	23444.01	Ovarian array	2559-2618
DEX0455_056.nt.2	2661	2661.0	Lung array	3287-3346
DEX0455_056.nt.2	3161	3161.0	Lung array	2518-2577
DEX0455_056.nt.2	1582	1582.0	Lung array	3081-3140
DEX0455_056.nt.2	22734	22734.02	Ovarian array	3081-3140
DEX0455_056.nt.2	3160	3160.0	Lung array	2559-2618
DEX0455_056.nt.2	18520	18520.02	Ovarian array	3081-3140
DEX0455_056.nt.2	3165	3165.0	Lung array	3041-3100
DEX0455_056.nt.2	1583	1583.0	Lung array	3041-3100
DEX0455_056.nt.2	3164	3164.0	Lung array	3081-3140
DEX0455_057.nt.1	7613	7613.0	Lung array	292-351
DEX0455_057.nt.1	33332	33332.02	Prostate1 array	600-659
DEX0455_057.nt.1	7612	7612.0	Lung array	381-440
DEX0455_057.nt.1	24524	24524.02	Ovarian array	600-659
DEX0455_057.nt.2	7613	7613.0	Lung array	458-517
DEX0455_057.nt.2	7612	7612.0	Lung array	547-606
DEX0455_057.nt.2	33332	33332.02	Prostate1 array	766-825
DEX0455_058.nt.1	14656	14656.02	Ovarian array	555-614
DEX0455_059.nt.1	17372	17372.01	Ovarian array	1778-1837
DEX0455_059.nt.1	11469	11469.02	Ovarian array	424-483
DEX0455_059.nt.1	17370	17370.01	Ovarian array	957-1016
DEX0455_059.nt.2	17372	17372.01	Ovarian array	1489-1548
DEX0455_059.nt.2	11469	11469.02	Ovarian array	424-483
DEX0455_060.nt.1	10372	10372.01	Ovarian array	1201-1260
DEX0455_060.nt.1	18582	18582.01	Ovarian array	672-731
DEX0455_061.nt.1	78508	78508.0	Multi-Cancer array	3736-3795
DEX0455_061.nt.1	103529	103529.01	Ovarian array	3740-3799
DEX0455_061.nt.1	19803	19803.0	Colon array	3736-3795
DEX0455_061.nt.1	96523	96523.02	Ovarian array	3740-3799
DEX0455_061.nt.1	19804	19804.0	Colon array	3684-3743
DEX0455_061.nt.2	19803	19803.0	Colon array	4690-4749
DEX0455_061.nt.2	78508	78508.0	Multi-Cancer array	4690-4749
DEX0455_061.nt.2	19804	19804.0	Colon array	4638-4697
DEX0455_061.nt.2	103529	103529.01	Ovarian array	4694-4753
DEX0455_061.nt.2	96523	96523.02	Ovarian array	4694-4753
DEX0455_061.nt.3	19803	19803.0	Colon array	4556-4615
DEX0455_061.nt.3	78508	78508.0	Multi-Cancer array	4556-4615
DEX0455_061.nt.3	103529	103529.01	Ovarian array	4560-4619
DEX0455_061.nt.3	19804	19804.0	Colon array	4504-4563
DEX0455_061.nt.3	96523	96523.02	Ovarian array	4560-4619
DEX0455_061.nt.4	103529	103529.01	Ovarian array	1702-1761
DEX0455_061.nt.4	19804	19804.0	Colon array	1646-1705
DEX0455_061.nt.4	78508	78508.0	Multi-Cancer array	1698-1757

DEX0455_061.nt.4	19803	19803.0	Colon array	1698-1757
DEX0455_061.nt.4	96523	96523.02	Ovarian array	1702-1761
DEX0455_061.nt.5	78508	78508.0	Multi-Cancer array	2394-2453
DEX0455_061.nt.5	103529	103529.01	Ovarian array	2398-2457
DEX0455_061.nt.5	19803	19803.0	Colon array	2394-2453
DEX0455_061.nt.5	19804	19804.0	Colon array	2342-2401
DEX0455_061.nt.5	96523	96523.02	Ovarian array	2398-2457
DEX0455_062.nt.1	18094	18094.01	Ovarian array	914-973
DEX0455_062.nt.1	17464	17464.02	Ovarian array	1167-1226

Example 2b: Relative Quantitation of Gene Expression

Real-Time quantitative PCR with fluorescent Taqman® probes is a quantitation detection system utilizing the 5'- 3' nuclease activity of Taq DNA polymerase. The method uses an internal fluorescent oligonucleotide probe (Taqman®) labeled with a 5' reporter dye and a downstream, 3' quencher dye. During PCR, the 5'-3' nuclease activity of Taq DNA polymerase releases the reporter, whose fluorescence can then be detected by the laser detector of the Model 7700 Sequence Detection System (PE Applied Biosystems, Foster City, CA, USA). Amplification of an endogenous control is used to standardize the amount of sample RNA added to the reaction and normalize for Reverse Transcriptase (RT) efficiency. Either cyclophilin, glyceraldehyde-3-phosphate dehydrogenase (GAPDH), ATPase, or 18S ribosomal RNA (rRNA) is used as this endogenous control. To calculate relative quantitation between all the samples studied, the target RNA levels for one sample were used as the basis for comparative results (calibrator). Quantitation relative to the "calibrator" can be obtained using the comparative method (User Bulletin #2: ABI PRISM 7700 Sequence Detection System).

The tissue distribution and the level of the target gene are evaluated for every sample in normal and cancer tissues. Total RNA is extracted from normal tissues, cancer tissues, and from cancers and the corresponding matched adjacent tissues. Subsequently, first strand cDNA is prepared with reverse transcriptase and the polymerase chain reaction is done using primers and Taqman® probes specific to each target gene. The results are analyzed using the ABI PRISM 7700 Sequence Detector. The absolute numbers are relative levels of expression of the target gene in a particular tissue compared to the calibrator tissue.

One of ordinary skill can design appropriate primers. The relative levels of expression of the OSNA versus normal tissues and other cancer tissues can then be

determined. All the values are compared to the calibrator. Normal RNA samples are commercially available pools, originated by pooling samples of a particular tissue from different individuals.

The relative levels of expression of the OSNA in pairs of matched samples may also be determined. A matched pair is formed by mRNA from the cancer sample for a particular tissue and mRNA from the normal adjacent sample for that same tissue from the same individual. All the values are compared to the calibrator.

In the analysis of matching samples, the OSNAs show a high degree of tissue specificity for the tissue of interest. These results confirm the tissue specificity results obtained with normal pooled samples. Further, the level of mRNA expression in cancer samples and the isogenic normal adjacent tissue from the same individual are compared. This comparison provides an indication of specificity for the cancer state (*e.g.* higher levels of mRNA expression in the cancer sample compared to the normal adjacent).

Informaton on the samples tested in the QPCR experiments below include the Sample ID (Smpl ID), Organ, Tissue Type (Tiss Type), Diagnosis (DIAG), Disease Detail, and Stage or Grade (STG or GRD) in following table.

Sample ID	ORGAN	TISS TYPE	DIAGNOSIS	DISEASE DETAIL	STAGE OR GRADE
A084	Ovary	CAN	Mucinous borderline tumor		
A084	Ovary	NAT	NAT		
G010	Ovary	CAN	Adenocarcinoma	Adenocarcinoma	Stage III
G010	Ovary	NAT		NAT	
G021	Ovary	CAN	Carcinoma	St. IIIC, poorly diff.	Stage-IIIC, poorly diff.
G021	Ovary	NAT		NAT	
1157	Ovary	CAN		malignant tumor	
7730	Ovary	CAN	Papillary adenocarcinoma	serous papillary adenocarcinoma	metastatic
8140	Ovary	CAN		Papillary Serous Adenocarcinoma	Stage IV
C360	Ovary	CAN	Adenocarcinoma	endometrioid adenocarcinoma	
10050	Ovary	CAN		papillary serous and endometrioid ovarian carcinoma, concurrent metastatic breast cancer	3
10400	Ovary	CAN		papillary serous adeno, metastatic	

1050	Ovary	CAN		Papillary Serous Carcinoma with Focal Mucinous Differentiation	Stage IC G0; T1cN0M0
130X	Ovary	CAN		Ovarian cancer	
7180	Ovary	CAN	Adenocarcinoma	malignant tumor	IIIC
A1B	Ovary	CAN	Adenocarcinoma	CA	
988Z	Ovary	CAN		papillary serous adenocarcinoma	poorly diff, FIGO IIIC
4510	Ovary	NRM		Normal Tissue	
247A	Ovary	NRM		NL	
35GA	Ovary	NRM		NL	
C087	Ovary	NRM		NL	
C109	Ovary	NRM		NL	
206I	Ovary	NRM		NL	
5150	Ovary	NRM		Normal	
18GA	Ovary	NRM		NL	
3370	Ovary	NRM		Normal	
1230	Ovary	NRM		Normal	
C177	Ovary	NRM		several fluid filled cysts	
40G	Ovary	NRM		NL	
C004	Ovary	NRM		NL	
030B	Urinary Bladder	CAN	Carcinoma	invasive Carcinoma,poorly differentiated	Stage III, Grade 3
030B	Urinary Bladder	NAT		NAT	
TR17	Urinary Bladder	CAN	Carcinoma	transitional cell carcinoma	StageII/GradeIII
TR17	Urinary Bladder	NAT		NAT	
520B	Urinary Bladder	CAN	Sarcomatoid transitional cell carcinoma	Sarcomatoid transitional cell carcinoma	
520B	Urinary Bladder	NAT		NAT	
401C	Colon	CAN	Adenocarcinoma	Adenocarcinoma of ascending colon and cecum	Stage III
401C	Colon	NAT		NAT	
AS43	Colon	CAN	Adenocarcinoma	malignant	
AS43	Colon	NAT	Adenocarcinoma	NAT	
AS98	Colon	CAN	Adenocarcinoma	Moderately to poorly differentiated adenocarcinoma	Duke's C
AS98	Colon	NAT		NAT	
CM12	Colon	CAN		T	Stage D
CM12	Colon	NAT	Adenocarcinoma	Nat	
DC19	Colon	CAN		T	Stage B
DC19	Colon	NAT		NL	
RC01	Colon	CAN	Cancer		Stage IV
RC01	Colon	NAT		NAT	

RS53	Colon	CAN	Adenocarcinoma	moderately differentiated adenocarcinoma	
RS53	Colon	NAT	Adenocarcinoma	NAT	
SG27	Colon	CAN		malig	Stage B
SG27	Colon	NAT		NAT	
TX01	Colon	CAN	Adenocarcinoma	Moderately differentiated adenocarcinoma of cecum	Stage II; T3NoMo
TX01	Colon	NAT		NAT	
KS52	Cervix	CAN	Squamous cell carcinoma	Keratinizing Squamous Cell Carcinoma	IIIB, well diff. G1; T3bNxM0
KS52	Cervix	NAT		NAT	
NK23	Cervix	CAN		Nonkeratinizing Large Cell	FIGO IIIB, undiff. G4; T3bNxM0
NK23	Cervix	NAT		NAT	
NKS54	Cervix	CAN	Squamous cell carcinoma	Nonkeratinizing Squamous Cell Carcinoma	IIB, mod diff. G2; T2bNxM0
NKS54	Cervix	NAT		NAT	
NKS55	Cervix	CAN	Squamous cell carcinoma	Nonkeratinizing Squamous Cell Carcinoma	IIIB, Mod diff. G2; T3bNxM0
NKS55	Cervix	NAT		NAT	
NKS81	Cervix	CAN	Squamous cell carcinoma	large cell nonkeratinizing sq carc, IIB, moderately diff	IIB
NKS81	Cervix	NAT		NAT	
NKS25	Cervix	CAN			
NKS25	Cervix	NAT		NAT	
NKS18	Cervix	CAN	Squamous cell carcinoma	Nonkeratinizing squamous cell carcinoma	GII
NKS18	Cervix	NAT		NAT	
10479	Endometrium	CAN		malignant mixed mullerian tumor	T?, Nx, M1
10479	Endometrium	NAT		NAT	
28XA	Endometrium	CAN	Endometrial adenocarcinoma	malignant	II/III
28XA	Endometrium	NAT		NAT	II/III
8XA	Endometrium	CAN	mod. diff, invasive, squamous differentiation, FIGO-II		
8XA	Endometrium	NAT		NAT	
106XD	Kidney	CAN	Renal cell carcinoma	renal cell carcinoma, clear cell, localized	3
106XD	Kidney	NAT		NL	

107XD	Kidney	CAN	Renal cell carcinoma	renal cell carcinoma, clear cell, with metastatic	G III
107XD	Kidney	NAT		NL	
109XD	Kidney	CAN		Malignant	G III
109XD	Kidney	NAT		NL	
10XD	Kidney	CAN	Renal cell carcinoma	renal cell carcinoma, clear cell, localized, grade 2-3	3
10XD	Kidney	NAT		NL	
22K	Kidney	CAN	Renal cell carcinoma	Renal cell carcinoma	G2, Mod. Diff.
22K	Kidney	NAT		NAT	
12XD	Kidney	CAN	Renal cell carcinoma	Left renal cell carcinoma	
12XD	Kidney	NAT		NAT	
15XA	Liver	CAN		Sarcoma,Retroper itoneal Tumor	Grade-2
15XA	Liver	NAT		CA	St. I, G4
174L	Liver	CAN	Hepatocellular carcinoma	Moderate to well differentiated hepatocellular carcinoma	
174L	Liver	NAT	Hepatocellular carcinoma	NAT	
187L	Liver	CAN	Adenocarcinoma	Metastatic Adenocarcinoma	Liver (Gallbladd er)
187L	Liver	NAT		NAT	
205L	Lung	CAN	Adenocarcinoma	poorly differentiated adenocarcinoma	T2, N1, Mx
205L	Lung	NAT		NAT	
315L	Lung	CAN	Squamous cell carcinoma		
315L	Lung	NAT	Adenocarcinoma	NAT	
507L	Lung	CAN	Bronchioloalveol ar carcinoma	bronchioalveolar carcinoma	Stage IB, G1, well diff.
507L	Lung	NAT		NAT	
528L	Lung	CAN	Adenocarcinoma	Adenocarcinoma	St.IV,T2N0 M1, infiltrati ng poorly diff.
528L	Lung	NAT		NAT	
8837L	Lung	CAN	Squamous cell carcinoma	Squamous cell carcinoma	T2, N0, M0
8837L	Lung	NAT		NAT	
AC11	Lung	CAN	Adenocarcinoma	poorly differentiated adenocarcinoma	T2, N2, M1
AC11	Lung	NAT		NAT	
AC39	Lung	CAN	Adenocarcinoma	intermediate grade adnocarcinoma	T2, N2, Mx
AC39	Lung	NAT		NAT	

SQ80	Lung	CAN	Squamous cell carcinoma	poorly differentiated squamous cell carcinoma	T1, N1, M0
SQ80	Lung	NAT		NAT	
SQ81	Lung	CAN	Squamous cell carcinoma	poorly differentiated squamous carcinoma	T3, N1, Mx
SQ81	Lung	NAT		NAT	
19DN	Mammary	CAN	Invasive ductal carcinoma	Invasive ductal carcinoma	G3, Stage IIA; T2N0M0
19DN	Mammary	NAT		NAT	
42DN	Mammary	CAN	Invasive ductal carcinoma	Invasive Ductal Carcinoma	T3aN1M0 IIIA, G3
42DN	Mammary	NAT		NAT	
517	Mammary	CAN	Infiltrating ductal carcinoma	Infiltrating ductal carcinoma	St. IIA, G3
517	Mammary	NAT		NAT	
781M	Mammary	CAN	Invasive ductal carcinoma		Architectural grade-3/3,Nuclear grade-3/3
781M	Mammary	NAT		NAT	
869M	Mammary	CAN	Invasive carcinoma	Invasive Carcinoma	Stage IIA G1; T2NoMo
869M	Mammary	NAT		NAT	
976M	Mammary	CAN	Invasive ductal carcinoma	Invasive Ductal Carcinoma	T2N1M0 (Stage 2B Grade 2-3)
976M	Mammary	NAT		NAT	
S570	Mammary	CAN	Carcinoma	Carcinoma	Stage IIA;T1N1Mo
S570	Mammary	NAT		NAT	
S699	Mammary	CAN	Invasive lobular carcinoma	Invasive Lobular Carcinoma	Stage IIB G1;T2N1Mo
S699	Mammary	NAT		NAT	
S997	Mammary	CAN	Invasive ductal carcinoma	Invasive Ductal Carcinoma	Stage IIB G3; T2N1Mo
S997	Mammary	NAT		NAT	
71XL	Pancreas	CAN		villous adenoma with paneth cell metaplasia	localized
71XL	Pancreas	NAT		NL	
82XP	Pancreas	CAN		serious cystadenoma	
82XP	Pancreas	NAT		NL	
92X	Pancreas	CAN	Ductal adenocarcinoma	ductal adenocarcinoma	mod to focally poorly diff.
92X	Pancreas	NAT		NL	
77X	Pancreas	CAN	Hepatic adenoma	Hepatic adenoma	
77X	Pancreas	NAT		NL	
23B	Prostate	CAN		Prostate tumor	Gleason's 3+4

23B	Prostate	NAT		NAT	
65XB	Prostate	CAN	Adenocarcinoma	adenocarcinom	3+4=7
65XB	Prostate	NAT		NL	
675P	Prostate	CAN	Adenocarcinoma	adenocarcinoma	
675P	Prostate	NAT		Normal	
84XB	Prostate	CAN	Adenocarcinoma	adenocarcinom	2+3
84XB	Prostate	NAT		NL	
958P	Prostate	CAN	Adenocarcinoma	Adenocarcinoma	T2C, NO, MX
958P	Prostate	NAT	NAT	Normal	
263C	Prostate	BPH		BPH	
276P	Prostate	BPH		BPH	
767B	Prostate	BPH		prostate BPH	
855P	Prostate	BPH		BPH	
10R	Prostate	PROST		active chronic prostatitis	T0, N0, M0
20R	Prostate	PROST		PROSTATITIS	
287S	Skin	CAN	Squamous cell carcinoma	Invasive Keratinizing Squamous Cell Carcinoma	Moderately Differentiated
287S	Skin	NAT		NAT	
39A	Skin	CAN		CA	St. II
39A	Skin	NAT		CA	St. II
669S	Skin	CAN	Melanoma	Nodular malignant melanoma	
669S	Skin	NAT		NAT	
171S	Small Intestine	CAN	Adenocarcinoma	Moderately differentiated Adenocarcinoma, invasive	
171S	Small Intestine	NAT		NAT	
20SM	Small Intestine	CAN	Adenocarcinoma	Adenocarcinoma, metastic to lung & liver	St. IV, poorly diff.
20SM	Small Intestine	NAT		NAT	
H89	Small Intestine	CAN	Adenocarcinoma	Adenocarcinoma	80% tumor, 50% necrosis, moderately differentiated, G2-3; T3N1MX
H89	Small Intestine	NAT	Adenocarcinoma	NAT	
261S	Stomach	CAN	Signet-ring cell carcinoma	Signet-ring cell carcinoma	Stage IIIA, T3N1M0
261S	Stomach	NAT		NAT	
288S	Stomach	CAN	Adenocarcinoma	Infiltrating Adneocarcinoma	Moderately Differentiated
288S	Stomach	NAT		NAT	

AC93 or 509L	Stomach	CAN	Adenocarcinoma	Adenocarcinoma	St. IV, G4, T4N3M0, poorly diff.
AC93 or 509L	Stomach	NAT		NAT	
88S	Stomach	CAN	Adenocarcinoma	Mucinous adenocarcinoma	T3N1M0, St. IIIA
88S	Stomach	NAT		NAT	
143N	Thyroid Gland	CAN	Follicular carcinoma	Follicular Carcinoma	
143N	Thyroid Gland	NAT		NAT	
270T	Thyroid Gland	CAN		CA	
270T	Thyroid Gland	NAT		NAT	
56T	Thyroid Gland	CAN	Papillary carcinoma	Papillary Carcinoma	St. III; T4N1M0
56T	Thyroid Gland	NAT		NAT	
39X	Testes	CAN		CA	
39X	Testes	NAT		NAT	
647T	Testes	CAN	Teratocarcinoma	Teratocarcinoma	Stage IA
647T	Testes	NAT	Teratocarcinoma	NAT	
663T	Testes	CAN	Teratocarcinoma	Teratocarcinoma	
663T	Testes	NAT		NAT	
135XO	Uterus	CAN		Uterus normal	
135XO	Uterus	NAT		Uterus tumor	
85XU	Uterus	CAN		endometrial carcinoma	I
85XU	Uterus	NAT		NL	
B1	Blood	NRM		Normal	
B3	Blood	NRM		Normal	
B5	Blood	NRM		Normal	
B6	Blood	NRM		Normal	
B11	Blood	NRM		Normal	
982B	Blood	NRM		Normal	
B69	Blood	NRM		Normal	
B72	Blood	NRM		Normal	
B73	Blood	NRM		Normal	
B75	Blood	NRM		Normal	
48AD	Adrenal Gland	NRM		Normal	
10BR	Brain	NRM		Normal	
01CL	Colon	NRM		Normal	
06CV	Cervix	NRM		Normal	
01ES	Esophagus	NRM		Normal	
46HR	Heart	NRM		Normal	
00HR	Human Reference	CAN	CAN	Cancer pool	
55KD	Kidney	NRM		Normal	
89LV	Liver	NRM		Normal	
90LN	Lung	NRM		Normal	
01MA	Mammary	NRM		Normal	

84MU	Skeletal Muscle	NRM		Normal	
3APV	Ovary	NRM		Normal	
04PA	Pancreas	NRM		Normal	
59PL	Placenta	NRM		Normal	
09PR	Prostate	NRM		Normal	
21RC	Rectum	NRM		Normal	
59SM	Small Intestine	NRM		Normal	
7GSP	Spleen	NRM		Normal	
09ST	Stomach	NRM		Normal	
4GTS	Testes	NRM		Normal	
99TM	Thymus Gland	NRM		Normal	
16TR	Trachea	NRM		Normal	
57UT	Uterus	NRM		Normal	

DEX0455_019.nt.1 (Ovr224)

The relative expression level of Ovr224 in various tissue samples is included below. Tissue samples include 68 pairs of matching samples, 10 non matched cancer samples, and 39 normal samples, all from various tissues annotated in the table. A matching pair is formed by mRNA from the cancer sample for a particular tissue and mRNA from the normal adjacent sample for that same tissue from the same individual. Of the normal samples 4 were blood samples which measured the expression levels in blood cells. Additionally, 2 prostatitis, and 4 Benign Prostatic Hyperplasia (BPH) samples are included. All the values are compared to ovarian cancer sample OVR7730 (calibrator).

The table below contains the relative expression level values for the sample as compared to the calibrator. The table includes the Sample ID, and expression level values for the following samples: Cancer (CAN), Normal Adjacent Tissue (NAT), Normal Tissue (NRM), Benign Prostatic Hyperplasia (BPH), and Prostatitis (PROST).

Sample ID	CAN	NAT	NRM	BPH	PROST
OVRA084	0.01	0.00			
OVRG010	0.00	0.06			
OVRG021	0.03	0.03			
OVR1157	0.36				
OVR7730	1.00				
OVR8140	0.02				
OVRC360	0.02				
OVR10050	0.35				
OVR10400	0.10				
OVR1050	0.00				
OVR130X	0.44				
OVR7180	0.02				
OVRA1B	0.04				

OVR247A			0.00		
OVR35GA			0.00		
OVRC087			0.00		
OVRC109			0.00		
OVR206I			0.00		
OVR515O			0.00		
OVR18GA			0.00		
OVR337O			0.00		
OVR123O			0.00		
OVRC177			0.02		
OVR40G			0.00		
OVRC004			0.00		
BLD030B	0.00	0.00			
BLDTR17	0.00	0.03			
CLN401C	0.00	0.00			
CLNAS98	0.02	0.00			
CLNCM12	0.00	0.02			
CLNDC19	0.02	0.00			
CLNRC01	0.00	0.01			
CLNRS53	0.14	0.00			
CLNSG27	0.00	0.00			
CLNTX01	0.00	0.00			
CVXKS52	0.00	0.03			
CVXNK23	0.01	0.00			
CVXNKS54	0.00	0.25			
CVXNKS55	0.06	0.17			
CVXNKS81	0.87	0.00			
ENDO10479	0.03	0.00			
ENDO28XA	0.00	0.00			
ENDO8XA	0.02	0.00			
KID106XD	0.00	0.08			
KID107XD	0.00	0.07			
KID109XD	0.06	0.37			
KID10XD	0.00	0.02			
KID22K	0.00	0.00			
LNG205L	0.00	0.33			
LNG315L	0.00	0.53			
LNG507L	0.21	0.43			
LNG528L	0.00	2.39			
LNG8837L	0.02	0.13			
LNGAC11	0.32	0.23			
LNGSQ80	0.00	0.00			
LVR187L	0.00	0.04			
MAM19DN	0.00	0.00			
MAM42DN	0.13	0.00			
MAM517	0.62	0.00			
MAM781M	0.00	0.00			

MAM869M	0.00	0.42			
MAM976M	0.00	0.00			
MAMS570	0.00	0.00			
MAMS699	0.00	0.00			
MAMS997	0.00	0.00			
PAN71XL	0.01	0.04			
PAN82XP	0.01	0.00			
PAN92X	0.00	0.00			
PRO23B	0.02	0.03			
PRO65XB	0.01	0.02			
PRO675P	0.07	0.00			
PRO84XB	0.02	0.09			
PRO958P	0.00	0.04			
PRO263C				0.00	
PRO276P				0.00	
PRO767B				0.04	
PRO855P				0.00	
PRO10R					0.00
PRO20R					0.00
SKN287S	0.00	0.00			
SKN39A	0.62	0.73			
SKN669S	0.02	0.00			
SMINT171S	0.00	0.00			
SMINT20SM	0.04	0.00			
SMINTH89	0.01	0.00			
STO261S	0.00	0.00			
STO288S	0.00	0.03			
STO88S	0.04	0.03			
THRD143N	0.00	0.04			
THRD270T	0.05	0.03			
THRD56T	0.44	0.05			
TST39X	0.00	0.33			
TST647T	0.02	0.07			
TST663T	0.05	0.01			
UTR135XO	0.05	0.00			
UTR85XU	0.03	0.00			
BLOB1			9.03		
BLOB3			0.71		
BLOB6			5.37		
BLOB11			3.85		
BLO982B			0.93		
ADR48AD			0.00		
BRN10BR			0.00		
CLN01CL			0.00		
ES001ES			0.22		
HRT46HR			0.00		
HUMREF00HR	0.00				

KID55KD			0.03		
LVR89LV			0.00		
LNG90LN			0.01		
MAM01MA			0.00		
MSL84MU			0.00		
OVR3APV			0.01		
PAN04PA			0.00		
PLA59PL			0.00		
PRO09PR			0.00		
REC21RC			0.00		
SMINT59SM			0.01		
SPL7GSP			0.63		
STO09ST			0.00		
THYM99TM			0.00		
TRA16TR			0.00		
TST4GTS			0.03		
UTR57UT			0.00		

Note: 0.00= Negative or Not Detected

The sensitivity for Ovr224 expression was calculated for the cancer samples versus normal samples. The sensitivity value indicates the percentage of cancer samples that show levels of Ovr224 at least 2 fold higher than the normal tissue or the corresponding normal adjacent form the same patient.

This specificity is an indication of the level of ovary tissue specific expression of the transcript compared to all the other tissue types tested in our assay. Thus, these experiments indicate Ovr224 being useful as an ovarian cancer diagnostic marker and/or therapeutic target.

Sensitivity and specificity data is reported in the table below.

	CLN	LNG	MAM	OVR	PRO
Sensitivity, Up vs. NAT	44%	0%	22%	0%	20%
Sensitivity, Down vs. NAT	22%	56%	11%	0%	40%
Sensitivity, Up vs. NRM	44%	33%	22%	92%	80%
Sensitivity, Down vs. NRM	0%	44%	0%	0%	0%
Specificity	47.03%	54.59%	45.41%	56%	52.41%

Altogether, the tissue specificity, plus the mRNA differential expression in the samples tested are believed to make Ovr224 a good marker for diagnosing, monitoring, staging, imaging and/or treating ovarian cancer.

Primers used for QPCR Expression Analysis of Ovr224 are as follows:
(Ovr224_forward): TCCTCAAGGGCCCTCCCCAG (SEQ ID NO:296)
(Ovr224_reverse): CCACAGCCATCTCCTCCATATTCTG (SEQ ID NO:297)
(Ovr224_probe): AAGTGTTCCTCTGGATGACCTACCTGG (SEQ ID NO:298)

DEX0455_031.nt.2 (Cln257)

The relative expression level of Cln257 in various tissue samples is included below. Tissue samples include 78 pairs of matching samples, 6 non matched cancer samples, and 35 normal samples, all from various tissues annotated in the table. A matching pair is formed by mRNA from the cancer sample for a particular tissue and mRNA from the normal adjacent sample for that same tissue from the same individual. Of the normal samples 5 were blood samples which measured the expression levels in blood cells. Additionally, 2 prostatitis, and 4 Benign Prostatic Hyperplasia (BPH) samples are included. All the values are compared to normal colon sample CLN01CL (calibrator).

The table below contains the relative expression level values for the sample as compared to the calibrator. The table includes the Sample ID, and expression level values for the following samples: Cancer (CAN), Normal Adjacent Tissue (NAT), Normal Tissue (NRM), Benign Prostatic Hyperplasia (BPH), and Prostatitis (PROST).

Sample ID	CAN	NAT	NRM	BPH	PROST
CLNAS12	5.55	10.39			
CLNAS46	6.28	3.22			
CLNB34	1.78	3.88			
CLNC9XR	2.76	3.35			
CLNCM67	2.91	2.44			
CLNTX89	6.56	5.08			
CLNAS43	27.92	6.39			
CLNAS98	6.93	5.42			
CLNRS53	8.04	6.77			
CLNRC01	9.91	2.51			
CLNSG27	4.56	7.39			
CLNDC19	3.97	3.84			
CLN401C	7.09	4.98			
CLNCM12	3.28	6.25			
CLNTX01	16.34	8.61			
BLD030B	2.29	2.59			
BLD520B	12.82	14.74			
BLDTR17	10.50	5.28			
CVXKS52	12.36	17.89			

CVXNK23	12.42	62.77			
CVXNKS54	24.16	13.33			
CVXNKS55	15.58	17.45			
CVXNKS81	84.82	132.51			
ENDO10479	15.86	25.40			
ENDO28XA	12.96	13.04			
ENDO8XA	12.25	3.60			
KID106XD	0.32	1.89			
KID107XD	29.14	4.27			
KID109XD	8.21	5.31			
KID10XD	5.61	0.84			
KID22K	2.84	1.47			
LNG205L	8.83	9.05			
LNG315L	16.63	28.85			
LNG507L	13.87	27.96			
LNG528L	20.05	27.89			
LNG8837L	16.21	10.02			
LNGAC11	15.21	14.83			
LNGAC39	49.00	16.41			
LNGSQ80	18.40	11.35			
LNGSQ81	7.80	54.12			
LVR15XA	9.04	2.93			
LVR174L	4.08	6.13			
LVR187L	3.52	3.60			
MAM19DN	14.68	14.78			
MAM42DN	12.41	26.01			
MAM517	133.69	12.41			
MAM781M	23.89	12.22			
MAM869M	7.84	17.28			
MAM976M	39.22	32.92			
MAMS570	21.06	26.04			
MAMS699	6.70	0.00			
MAMS997	11.37	13.47			
OVRG021	9.65	18.53			
OVR10050	36.75				
OVR10400	14.88				
OVR1050	8.82				
OVR130X	32.30				
OVR7180	22.87				
OVRA1B	15.50				
OVR1230			16.94		
OVR18GA			13.92		
OVR206I			15.98		

OVR337O			13.28		
OVR40G			20.23		
OVR515O			26.97		
OVRC004			54.21		
OVRC177			6.97		
PAN71XL	9.65	8.64			
PAN82XP	7.20	24.22			
PAN92X	8.74	26.55			
PRO23B	13.10	14.00			
PRO65XB	6.20	10.57			
PRO675P	20.64	27.15			
PRO84XB	10.46	10.35			
PRO958P	11.48	10.47			
PRO263C				35.87	
PRO276P				7.20	
PRO767B				17.09	
PRO855P				8.27	
PRO10R					16.92
PRO20R					15.27
SKN287S	8.51	9.87			
SKN39A	12.75	8.64			
SKN669S	8.95	23.59			
SMINT171S	9.57	15.19			
SMINT20SM	30.83	12.12			
SMINTH89	10.91	10.48			
STO261S	16.09	3.67			
STO288S	8.76	3.43			
STO88S	14.77	4.27			
THRD143N	6.43	17.06			
THRD270T	25.28	27.05			
THRD56T	12.28	9.55			
TST39X	7.03	1.37			
TST647T	4.87	5.35			
TST663T	10.23	3.49			
UTR135XO	10.47	13.31			
UTR85XU	25.28	27.08			
BLOB1			82.99		
BLOB3			15.84		

BLOB6			81.31		
BLOB11			12.68		
BLO982B			3.82		
ADR48AD			1.96		
HUMREF00HR	0.94				
BRN10BR			0.00		
CLN01CL			1.00		
ESO01ES			4.70		
HRT46HR			0.59		
KID55KD			0.58		
LVR89LV			1.93		
LNG90LN			3.14		
MAM01MA			6.01		
MSL84MU			0.21		
OVR3APV			5.62		
PAN04PA			3.59		
PLA59PL			5.14		
PRO09PR			3.40		
REC21RC			8.88		
SMINT59SM			3.09		
SPL7GSP			3.91		
STO09ST			2.19		
THYM99TM			4.39		
TRA16TR			6.32		
TST4GTS			1.10		
UTR57UT			14.36		

0.00= Negative or Not Detected

The sensitivity for Cln257 expression was calculated for the cancer samples versus normal samples. The sensitivity value indicates the percentage of cancer samples that show levels of Cln257 at least 2 fold higher than the normal tissue or the corresponding normal adjacent form the same patient.

This specificity is an indication of the level of colon tissue specific expression of the transcript compared to all the other tissue types tested in our assay. Thus, these experiments indicate Cln257 being useful as an colon cancer diagnostic marker and/or therapeutic target.

Sensitivity and specificity data is reported in the table below.

	CLN	LNG	MAM	OVR	PRO
Sensitivity, Up vs. NAT	13%	11%	22%	0%	0%

Sensitivity, Down vs. NAT	7%	22%	22%	0%	0%
Sensitivity, Up vs. NRM	93%	100%	67%	29%	80%
Sensitivity, Down vs. NRM	0%	0%	0%	0%	0%
Specificity	3.47 %	6.49 %	5.95 %	6.42 %	5.35 %

Altogether, the tissue specificity, plus the mRNA differential expression in the samples tested are believed to make Cln257 a good marker for diagnosing, monitoring, staging, imaging and/or treating colon cancer.

Primers used for QPCR Expression Analysis of Cln257 are as follows:
(Cln257_forward): CTGAAGCCGAGCTCAAAGGT (SEQ ID NO:299)
(Cln257_reverse): CCCTGCTCCCACTTGAGATC (SEQ ID NO:300)
(Cln257_probe): TGTGAAAAGGAGGCTGGGTGCCAG (SEQ ID NO:301)

<u>DEX0455_034.nt.1 and DEX0455_034.nt.2 (Ovr223)</u>

The relative expression level of Ovr223 in various tissue samples is included below. Tissue samples include 75 pairs of matching samples, 11 non matched cancer samples, and 39 normal samples, all from various tissues annotated in the table. A matching pair is formed by mRNA from the cancer sample for a particular tissue and mRNA from the normal adjacent sample for that same tissue from the same individual. Of the normal samples 4 were blood samples which measured the expression levels in blood cells. Additionally, 2 prostatitis, and 4 Benign Prostatic Hyperplasia (BPH) samples are included. All the values are compared to ovarian cancer sample OVR773O (calibrator).

The table below contains the relative expression level values for the sample as compared to the calibrator. The table includes the Sample ID, and expression level values for the following samples: Cancer (CAN), Normal Adjacent Tissue (NAT), Normal Tissue (NRM), Benign Prostatic Hyperplasia (BPH), and Prostatitis (PROST).

Sample ID	CAN	NAT	NRM	BPH	PROST
OVRA084	0.12	0.05			
OVRG010	0.04	0.24			
OVRG021	0.16	0.05			
OVR1157	0.32				
OVR773O	1.00				
OVR814O	0.06				
OVRC360	0.00				
OVR1005O	0.75				

OVR1040O	0.97				
OVR105O	0.80				
OVR130X	2.15				
OVR718O	0.80				
OVRA1B	1.90				
OVR247A			0.00		
OVR35GA			0.03		
OVRC087			0.06		
OVRC109			0.04		
OVR206I			0.00		
OVR515O			0.00		
OVR18GA			0.12		
OVR337O			0.00		
OVR123O			0.00		
OVRC177			0.03		
OVR40G			0.02		
OVRC004			0.00		
BLD030B	0.00	0.00			
BLD520B	0.74	0.02			
BLDTR17	0.00	0.11			
CLN401C	0.40	0.35			
CLNAS43	1.05	0.16			
CLNAS98	0.16	0.25			
CLNCM12	0.21	0.31			
CLNDC19	0.47	0.17			
CLNRC01	0.31	0.31			
CLNRS53	0.18	1.03			
CLNSG27	0.00	0.29			
CLNTX01	0.36	0.25			
CVXKS52	0.00	0.74			
CVXNK23	0.68	2.29			
CVXNKS54	1.18	2.21			
CVXNKS55	0.92	0.82			
CVXNKS81	1.72				
ENDO10479	0.48	1.16			
ENDO28XA	1.17	0.25			
ENDO8XA	0.52	0.13			
KID106XD	0.05	0.05			
KID107XD	0.00	0.21			
KID109XD	0.14	0.61			
KID10XD	0.00	0.06			
KID22K	0.21	0.10			
LNG205L	0.23	0.00			
LNG315L	0.15	2.19			
LNG507L	0.37	0.82			
LNG528L	2.95	0.60			
LNG8837L	0.45	0.70			

LNGAC11	0.17	0.54			
LNGAC39	1.86	0.23			
LNGSQ80	0.82	0.00			
LNGSQ81	1.06	0.69			
LVR174L	0.00	0.00			
LVR187L	0.00	0.29			
MAM19DN	1.16	0.87			
MAM42DN	0.60	0.00			
MAM517	7.70	0.00			
MAM781M	0.41	0.74			
MAM869M	0.58	0.00			
MAM976M	1.01	0.42			
MAMS570	2.29	4.07			
MAMS699	0.39	0.00			
MAMS997	1.33	0.86			
PAN71XL	0.44	0.77			
PAN82XP	0.10	7.85			
PAN92X	0.49	0.81			
PRO23B	0.15	0.19			
PRO65XB	0.20	0.52			
PRO675P	0.43	0.32			
PRO84XB	0.43	0.45			
PRO958P	0.46	0.52			
PRO263C				0.00	
PRO276P				0.13	
PRO767B				0.48	
PRO855P				0.28	
PRO10R					0.34
PRO20R					0.95
SKN287S	0.49	0.46			
SKN39A	0.00	0.16			
SKN669S	0.38	2.09			
SMINT171S	0.70	0.51			
SMINT20SM	0.83	0.31			
SMINTH89	0.43	1.27			
STO261S	1.61	0.52			
STO288S	0.39	0.16			
STO88S	0.00	0.18			
THRD143N	0.25	0.45			
THRD270T	0.95	2.10			
THRD56T	2.62	0.23			
TST39X	0.47	0.90			
TST647T	0.38	0.16			
TST663T	0.30	0.02			
UTR135XO	0.09	0.30			
UTR85XU	1.07	0.59			
BLOB1			0.00		

BLOB6			0.00		
BLOB11			0.95		
BLO982B			0.00		
ADR48AD			0.00		
BRN10BR			0.00		
CLN01CL			0.04		
CVX1ACV			7.20		
ESO01ES			0.56		
HRT46HR			0.00		
HUMREF00HR	0.00				
KID55KD			0.01		
LVR89LV			0.00		
LNG90LN			0.26		
MAM01MA			0.10		
MSL84MU			0.00		
OVR3APV			0.03		
PAN04PA			0.11		
PLA59PL			0.33		
PRO09PR			0.27		
REC21RC			0.18		
SMINT59SM			0.09		
SPL7GSP			0.06		
STO09ST			0.21		
THYM99TM			0.00		
TRA16TR			0.69		
TST4GTS			0.00		
UTR57UT			0.14		

0.00= Negative or Not Detected

The sensitivity for Ovr223 expression was calculated for the cancer samples versus normal samples. The sensitivity value indicates the percentage of cancer samples that show levels of Ovr223 at least 2 fold higher than the normal tissue or the corresponding normal adjacent form the same patient.

This specificity is an indication of the level of ovary tissue specific expression of the transcript compared to all the other tissue types tested in our assay. Thus, these experiments indicate Ovr223 being useful as an ovarian cancer diagnostic marker and/or therapeutic target.

Sensitivity and specificity data is reported in the table below.

	CLN	LNG	MAM	OVR	PRO
Sensitivity, Up vs. NAT	22%	44%	56%	0%	0%
Sensitivity, Down vs. NAT	22%	33%	0%	0%	20%
Sensitivity, Up vs. NRM	89%	44%	100%	85%	0%

Sensitivity, Down vs. NRM	11%	0%	0%	8%	0%
Specificity	24.32 %	25.41 %	30.81 %	22.86 %	25.67 %

Altogether, the tissue specificity, plus the mRNA differential expression in the samples tested are believed to make Ovr223 a good marker for diagnosing, monitoring, staging, imaging and/or treating ovarian cancer.

Additionally, the tissue specificity, plus the mRNA differential expression in the samples tested may make Ovr223 a good marker for diagnosing, monitoring, staging, imaging and/or treating breast cancer.

Primers used for QPCR Expression Analysis of Ovr223 are as follows:

(Ovr223_forward): AGTGAGAGGGTGGGCATGTATG (SEQ ID NO:302)

(Ovr223_reverse): TACTCCAGGCGCTCTGAGGAT (SEQ ID NO:303)

(Ovr223_probe): TTAGCCAGTGGCCTCCACTCTGTCCC (SEQ ID NO:304)

<u>DEX0455_034.nt.4 (Ovr223v2)</u>

The relative expression level of Ovr223v2 in various tissue samples is included below. Tissue samples include 74 pairs of matching samples, 11 non matched cancer samples, and 39 normal samples, all from various tissues annotated in the table. A matching pair is formed by mRNA from the cancer sample for a particular tissue and mRNA from the normal adjacent sample for that same tissue from the same individual. Of the normal samples 4 were blood samples which measured the expression levels in blood cells. Additionally, 2 prostatitis, and 4 Benign Prostatic Hyperplasia (BPH) samples are included. All the values are compared to normal pancreas sample PAN04PA (calibrator).

The table below contains the relative expression level values for the sample as compared to the calibrator. The table includes the Sample ID, and expression level values for the following samples: Cancer (CAN), Normal Adjacent Tissue (NAT), Normal Tissue (NRM), Benign Prostatic Hyperplasia (BPH), and Prostatitis (PROST).

Sample ID	CAN	NAT	NRM	BPH	PROST
OVRA084	0.25	0.00			
OVRG010	4.93				
OVRG021	0.40	0.06			
OVR1157	3.69				
OVR773O	7.06				
OVR988Z	1.93				
OVRC360	0.34				

OVR1005O	2.85				
OVR1040O	3.20				
OVR105O	3.02				
OVR130X	1.84				
OVR718O	2.15				
OVRA1B	7.99				
OVR247A			0.44		
OVR35GA			0.21		
OVRC087			0.23		
OVRC109			0.20		
OVR206I			0.11		
OVR515O			0.12		
OVR18GA			0.07		
OVR337O			0.20		
OVR123O			0.93		
OVRC177			0.10		
OVR40G			0.05		
OVR451O			0.32		
BLD030B	0.20	1.10			
BLD520B	2.00	0.18			
BLDTR17	0.39	1.04			
CLN401C	0.85	1.23			
CLNAS43	2.68	0.16			
CLNAS98	0.61	0.35			
CLNCM12	0.61	0.80			
CLNDC19	1.94	1.18			
CLNRC01	0.46	0.42			
CLNRS53	0.54	1.26			
CLNSG27	0.61	0.65			
CLNTX01	1.62	0.59			
CVXKS52	3.54	4.98			
CVXNKS55	7.35	4.40			
CVXNKS25	4.23	4.81			
CVXNKS18	1.26	3.88			
CVXNKS54	3.00	1.47			
ENDO10479	3.07	0.37			
ENDO28XA	4.24	0.69			
ENDO8XA	0.31	3.57			
KID106XD	0.11	0.33			
KID12XD	0.27	2.13			
KID10XD	0.10	0.21			
KID22K	0.60	0.28			
KID107XD	0.16	0.44			
LNG205L	0.81	1.09			
LNG315L	0.89	2.02			
LNG507L	1.16	1.68			
LNG528L	9.15	1.43			

LNG8837L	1.46	1.65			
LNGAC11	0.86	1.78			
LNGAC39	6.93	1.66			
LNGSQ80	1.13	0.32			
LNGSQ81	1.95	1.13			
LVR15XA	0.01	0.03			
LVR174L	0.00	0.01			
LVR187L	0.00	2.35			
MAM19DN	3.52	3.45			
MAM42DN	0.83	1.62			
MAM517	10.39	3.02			
MAM781M	1.80	0.34			
MAM869M	1.85	0.13			
MAM976M	4.08	0.67			
MAMS570	2.43	4.41			
MAMS699	1.16	1.50			
MAMS997	1.20	1.39			
PAN71XL	1.91	1.83			
PAN77X	0.00	0.02			
PAN92X	3.25	0.25			
PRO10R					2.41
PRO20R					1.07
PRO23B	1.32	1.17			
PRO263C				1.30	
PRO276P				0.88	
PRO65XB	0.87	1.60			
PRO675P	1.50	0.69			
PRO767B				4.10	
PRO84XB	1.41	1.13			
PRO855P				1.16	
PRO958P	2.49	2.56			
SKN287S	0.76	0.57			
SKN39A	0.25	0.20			
SKN669S	0.60	1.12			
SMINT171S	1.06	2.38			
SMINT20SM	3.20	1.14			
SMINTH89	1.92	1.80			
STO261S	3.86	0.75			
STO288S	1.00	0.23			
STOAC93	0.66	2.01			
STO88S	2.57	0.20			
THRD143N	1.77	1.15			
THRD270T	2.23	2.56			
THRD56T	3.02	0.40			
TST39X	0.80	0.77			
TST647T	1.15	0.43			
TST663T	0.55	0.05			

UTR135XO	0.58	0.52			
UTR85XU	2.70	1.49			
BLOB3			0.19		
BLOB11			0.93		
BLO69			0.10		
BLO72			0.06		
BLO73			0.13		
ADR48AD			0.15		
BRN10BR			0.00		
CLN01CL			1.03		
CVX06CV			0.48		
ESO01ES			3.34		
HRT46HR			0.01		
HUMREF00HR	0.08				
KID55KD			0.27		
LVR89LV			0.03		
LNG90LN			3.99		
MAM01MA			2.38		
MSL84MU			0.00		
OVR3APV			0.13		
PAN04PA			1.00		
PRO09PR			3.27		
REC21RC			2.01		
SMINT59SM			0.55		
SPL7GSP			0.46		
STO09ST			0.98		
THYM99TM			0.54		
TRA16TR			3.04		
TST4GTS			0.10		
UTR57UT			0.43		

0.00= Negative or Not Detected

The sensitivity for Ovr223v2 expression was calculated for the cancer samples versus normal samples. The sensitivity value indicates the percentage of cancer samples that show levels of Ovr223v2 at least 2 fold higher than the normal tissue or the corresponding normal adjacent form the same patient.

This specificity is an indication of the level of ovary tissue specific expression of the transcript compared to all the other tissue types tested in our assay. Thus, these experiments indicate Ovr223v2 being useful as an ovarian cancer diagnostic marker and/or therapeutic target.

Sensitivity and specificity data is reported in the table below.

	CLN	LNG	MAM	OVR	PRO
Sensitivity, Up vs. NAT	22%	33%	44%	0%	20%

Sensitivity, Down vs. NAT	11%	22%	0%	0%	0%
Sensitivity, Up vs. NRM	11%	11%	11%	85%	0%
Sensitivity, Down vs. NRM	11%	78%	22%	0%	80%
Specificity	8.06 %	12.9 %	16.67 %	19.77 %	14.89 %

Altogether, the tissue specificity, plus the mRNA differential expression in the samples tested are believed to make Ovr223v2 a good marker for diagnosing, monitoring, staging, imaging and/or treating ovarian cancer.

Primers used for QPCR Expression Analysis of Ovr223v2 are as follows:

(Ovr223v2_forward): TCCAGATGGCTCAGCTTCTTC (SEQ ID NO:305)

(Ovr223v2_reverse): GAAGGTGTTCGGAGAATGAGTGA (SEQ ID NO:306)

(Ovr223v2_probe): TTTCTTCTGTGGCTCTGTGTTTTCCAGGC (SEQ ID NO:307)

DEX0455_037.nt.6 (Ovr229)

The relative expression level of Ovr229 in various tissue samples is included below. Tissue samples include 74 pairs of matching samples, 10 non matched cancer samples, and 40 normal samples, all from various tissues annotated in the table. A matching pair is formed by mRNA from the cancer sample for a particular tissue and mRNA from the normal adjacent sample for that same tissue from the same individual. Of the normal samples 5 were blood samples which measured the expression levels in blood cells. Additionally, 2 prostatitis, and 4 Benign Prostatic Hyperplasia (BPH) samples are included. All the values are compared to normal prostate sample PRO09PR (calibrator).

The table below contains the relative expression level values for the sample as compared to the calibrator. The table includes the Sample ID, and expression level values for the following samples: Cancer (CAN), Normal Adjacent Tissue (NAT), Normal Tissue (NRM), Benign Prostatic Hyperplasia (BPH), and Prostatitis (PROST).

Sample ID	CAN	NAT	NRM	BPH	PROST
OVRA084	0.01	0.00			
OVRG010	0.36	0.00			
OVRG021	0.39	0.09			
OVR1157	0.00				
OVR773O	0.31				
OVR988Z	1.25				
OVRC360	1.64				

OVR1005O	0.47				
OVR1040O	1.49				
OVR105O	0.33				
OVR130X	0.00				
OVR718O	0.42				
OVRA1B	0.27				
OVR247A			0.00		
OVR35GA			0.05		
OVRC087			0.40		
OVRC109			0.00		
OVR206I			0.12		
OVR515O			0.42		
OVR18GA			0.00		
OVR337O			0.00		
OVR123O			0.00		
OVRC177			0.22		
OVR40G			0.00		
OVR451O			0.00		
BLD030B	0.04	0.14			
BLD520B	0.00	0.23			
BLDTR17	0.37	0.19			
CLN401C	0.04	0.04			
CLNAS43	0.10	0.14			
CLNAS98	0.00	0.00			
CLNCM12	0.11	0.12			
CLNDC19	0.00	0.09			
CLNRC01	0.01	0.02			
CLNRS53	0.00	0.00			
CLNSG27	0.08	0.31			
CLNTX01	0.00	0.24			
CVXKS52	0.00	0.35			
CVXNKS55	0.03	0.25			
CVXNKS25	1.68	0.25			
CVXNKS18	0.00	0.06			
CVXNKS54	0.00	1.22			
ENDO10479	0.13	0.35			
ENDO28XA	0.18	0.54			
ENDO8XA	0.00	0.05			
KID106XD	0.00	0.02			
KID12XD	0.01	0.37			
KID10XD	0.00	0.01			
KID22K	0.02	0.06			
KID107XD	0.00	0.02			
LNG205L	0.01	1.04			
LNG315L	0.14	1.69			
LNG507L	0.48	3.36			
LNG528L	0.00	0.71			

LNG8837L	0.12	1.08			
LNGAC11	0.10	0.20			
LNGAC39	0.52	2.65			
LNGSQ80	0.16	2.29			
LNGSQ81	0.23	2.01			
LVR15XA	0.00	0.03			
LVR174L	0.00	0.02			
LVR187L	0.00	0.00			
MAM19DN	0.00	0.28			
MAM42DN	0.17	0.00			
MAM517	2.59	0.00			
MAM781M	0.00	0.00			
MAM869M	0.05	0.74			
MAM976M	0.26	0.00			
MAMS570	0.00	0.00			
MAMS699	0.28	0.89			
MAMS997	0.13	0.23			
PAN71XL	0.06	0.09			
PAN77X	0.00	0.05			
PAN92X	0.27	0.00			
PRO10R					1.00
PRO20R					8.84
PRO23B	1.11	1.14			
PRO263C				1.16	
PRO276P				0.93	
PRO65XB	0.14	0.85			
PRO675P	0.42	0.51			
PRO767B				0.88	
PRO84XB	0.15	3.51			
PRO855P				2.76	
PRO958P	0.76	2.69			
SKN287S	0.22	2.01			
SKN39A	0.16	0.00			
SKN669S	0.40	0.00			
SMINT171S	0.02	0.04			
SMINT20SM	0.07	0.15			
SMINTH89	0.05	0.00			
STO261S	0.00	0.11			
STO288S	0.02	0.12			
STOAC93	0.23	0.05			
THRD143N	0.00	0.27			
THRD270T	0.09	0.07			
THRD56T	0.00	0.00			
TST39X	0.00	8.21			
TST647T	0.19	9.27			
TST663T	0.14	10.16			
UTR135XO	0.58	0.35			

UTR85XU	0.00	0.99			
BLOB3			0.00		
BLOB11			0.00		
BLO69			0.00		
BLO72			0.17		
BLO73			0.00		
ADR48AD			0.00		
BRN10BR			2.25		
CLN01CL			0.10		
CVX06CV			2.46		
ESO01ES			0.00		
HRT46HR			0.88		
HUMREF00HR	0.00				
KID55KD			0.02		
LVR89LV			0.03		
LNG90LN			0.03		
MAM01MA			0.02		
MSL84MU			0.02		
OVR3APV			0.08		
PAN04PA			0.29		
PLA59PL			1.46		
PRO09PR			1.00		
REC21RC			0.67		
SMINT59SM			0.04		
SPL7GSP			0.80		
STO09ST			0.10		
THYM99TM			0.46		
TRA16TR			0.15		
TST4GTS			12.18		
UTR57UT			1.54		

0.00= Negative or Not Detected

The sensitivity for Ovr229 expression was calculated for the cancer samples versus normal samples. The sensitivity value indicates the percentage of cancer samples that show levels of Ovr229 at least 2 fold higher than the normal tissue or the corresponding normal adjacent form the same patient.

This specificity is an indication of the level of ovary tissue specific expression of the transcript compared to all the other tissue types tested in our assay. Thus, these experiments indicate Ovr229 being useful as an ovarian cancer diagnostic marker and/or therapeutic target.

Sensitivity and specificity data is reported in the table below.

	CLN	LNG	MAM	OVR	PRO
Sensitivity, Up vs. NAT	0%	0%	33%	0%	0%

Sensitivity, Down vs. NAT	44%	100%	33%	0%	60%
Sensitivity, Up vs. NRM	0%	78%	67%	85%	0%
Sensitivity, Down vs. NRM	67%	22%	33%	0%	60%
Specificity	26.06 %	31.38 %	28.19 %	35.96 %	42.11 %

Altogether, the tissue specificity, plus the mRNA differential expression in the samples tested are believed to make Ovr229 a good marker for diagnosing, monitoring, staging, imaging and/or treating ovarian cancer.

Primers used for QPCR Expression Analysis of Ovr229 are as follows:

(Ovr229_forward): CCTGCCGCGGAGATCCAT (SEQ ID NO:308)

(Ovr229_reverse): GCAGCGCGTACTGGTCGTA (SEQ ID NO:309)

(Ovr229_probe): CCTACTCCGTGTCAGTGGTGGAG (SEQ ID NO:310)

DEX0455_037.nt.7 (Ovr227)

The relative expression level of Ovr227 in various tissue samples is included below. Tissue samples include 74 pairs of matching samples, 10 non matched cancer samples, and 39 normal samples, all from various tissues annotated in the table. A matching pair is formed by mRNA from the cancer sample for a particular tissue and mRNA from the normal adjacent sample for that same tissue from the same individual. Of the normal samples 5 were blood samples which measured the expression levels in blood cells. Additionally, 2 prostatitis, and 4 Benign Prostatic Hyperplasia (BPH) samples are included. All the values are compared to prostate normal sample PRO09PR (calibrator).

The table below contains the relative expression level values for the sample as compared to the calibrator. The table includes the Sample ID, and expression level values for the following samples: Cancer (CAN), Normal Adjacent Tissue (NAT), Normal Tissue (NRM), Benign Prostatic Hyperplasia (BPH), and Prostatitis (PROST).

Sample ID	CAN	NAT	NRM	BPH	PROST
OVRA084	1.31	0.24			
OVRG010	1.65	0.75			
OVRG021	0.87	0.00			
OVR1157	0.85				
OVR7730	0.21				
OVR8140	0.24				
OVRC360	0.58				
OVR10050	0.33				

OVR1040O	0.11				
OVR105O	0.12				
OVR130X	0.15				
OVR718O	0.32				
OVRA1B	0.11				
OVR247A			0.40		
OVR35GA			0.06		
OVRC087			0.16		
OVRC109			0.08		
OVR206I			0.00		
OVR515O			0.63		
OVR18GA			0.00		
OVR337O			0.00		
OVR123O			0.00		
OVRC177			0.03		
OVR40G			0.02		
OVRC004			0.00		
BLD030B	0.02	0.00			
BLD520B	0.00	0.06			
BLDTR17	0.00	0.00			
CLN401C	0.02	0.04			
CLNAS43	0.00	0.00			
CLNAS98	0.00	0.09			
CLNCM12	0.06	0.05			
CLNDC19	0.04	0.10			
CLNRC01	0.00	0.00			
CLNRS53	0.18	0.40			
CLNSG27	0.00	0.28			
CLNTX01	0.58	0.00			
CVXKS52	0.00	0.49			
CVXNK23	0.00	0.00			
CVXNKS54	1.12	2.58			
CVXNKS55	0.01	0.00			
CVXNKS81	0.00	0.00			
ENDO10479	0.00	2.93			
ENDO28XA	0.76	0.52			
ENDO8XA	0.03	0.00			
KID106XD	0.00	0.00			
KID107XD	0.00	0.04			
KID109XD	0.00	0.00			
KID10XD	0.21	0.02			
KID22K	0.01	0.02			
LNG205L	0.00	0.35			
LNG315L	0.33	1.50			
LNG507L	0.24	2.81			
LNG528L	0.00	0.42			
LNG8837L	0.18	1.12			

LNGAC11	0.20	0.04			
LNGAC39	0.59	1.37			
LNGSQ80	1.38	1.09			
LNGSQ81	0.65	1.59			
LVR15XA	0.00	0.02			
LVR174L	0.00	0.01			
LVR187L	0.00	0.09			
MAM19DN	0.00	0.07			
MAM42DN	0.16	0.00			
MAM517	0.00	0.00			
MAM781M	0.00	0.24			
MAM869M	0.00	0.00			
MAM976M	0.12	0.00			
MAMS570	0.00	0.00			
MAMS699	0.53	0.00			
MAMS997	0.20	0.11			
PAN71XL	0.00	0.03			
PAN82XP	0.00	0.00			
PAN92X	0.10	0.78			
PRO23B	0.35	0.20			
PRO65XB	0.05	0.61			
PRO675P	0.22	0.40			
PRO84XB	0.12	1.68			
PRO958P	0.18	0.31			
PRO263C				0.32	
PRO276P				0.21	
PRO767B				0.69	
PRO855P				0.29	
PRO10R					0.38
PRO20R					1.35
SKN287S	0.00	2.19			
SKN39A	0.17	0.00			
SKN669S	0.14	0.12			
SMINT171S	0.39	0.15			
SMINT20SM	0.06	0.07			
SMINTH89	0.01	0.00			
STO261S	0.60	0.18			
STO288S	0.03	0.04			
STO88S	0.00	0.07			
THRD143N	0.01	0.04			
THRD270T	0.03	0.03			
THRD56T	0.00	0.14			
TST39X	0.00	1.74			
TST647T	0.02	3.30			
TST663T	0.05	0.68			
UTR135XO	0.22	0.17			
UTR85XU	0.12	0.19			

BLOB1			7.89		
BLOB3			0.00		
BLOB6			0.00		
BLOB11			0.07		
BLO982B			2.25		
ADR48AD			0.00		
BRN10BR			1.02		
CLN01CL			0.00		
ESO01ES			0.25		
HRT46HR			0.10		
HUMREF00HR	0.00				
KID55KD			0.01		
LVR89LV			0.02		
LNG90LN			0.11		
MAM01MA			0.00		
MSL84MU			0.07		
OVR3APV			0.02		
PAN04PA			0.20		
PLA59PL			0.42		
PRO09PR			1.00		
REC21RC			0.28		
SMINT59SM			0.01		
SPL7GSP			1.33		
STO09ST			0.02		
THYM99TM			0.38		
TRA16TR			0.10		
TST4GTS			2.47		
UTR57UT			0.43		

0.00= Negative or Not Detected

The sensitivity for Ovr227 expression was calculated for the cancer samples versus normal samples. The sensitivity value indicates the percentage of cancer samples that show levels of Ovr227 at least 2 fold higher than the normal tissue or the corresponding normal adjacent form the same patient.

This specificity is an indication of the level of ovary tissue specific expression of the transcript compared to all the other tissue types tested in our assay. Thus, these experiments indicate Ovr227 being useful as an ovarian cancer diagnostic marker and/or therapeutic target.

Sensitivity and specificity data is reported in the table below.

	CLN	LNG	MAM	OVR	PRO
Sensitivity, Up vs. NAT	11%	11%	33%	0%	0%
Sensitivity, Down vs. NAT	67%	78%	22%	0%	40%

Sensitivity, Up vs. NRM	56%	56%	44%	100%	0%
Sensitivity, Down vs. NRM	0%	22%	0%	0%	100%
Specificity	28.11 %	40.54 %	25.41 %	42.86 %	39.04 %

Altogether, the tissue specificity, plus the mRNA differential expression in the samples tested are believed to make Ovr227 a good marker for diagnosing, monitoring, staging, imaging and/or treating ovarian cancer.

Primers used for QPCR Expression Analysis of Ovr227 are as follows:

(Ovr227_forward): AGAGGCGCCCCGCAGGTA (SEQ ID NO:311)

(Ovr227_reverse): CCCGGAGCCAGCTCGAGTT (SEQ ID NO:312)

(Ovr227_probe): CAGGAACTGCGGCGAGCGACCC (SEQ ID NO:313)

DEX0455_040.nt.2 (Ovr218)

The relative expression level of Ovr218 in various tissue samples is included below. Tissue samples include 75 pairs of matching samples, 10 non matched cancer samples, and 41 normal samples, all from various tissues annotated in the table. A matching pair is formed by mRNA from the cancer sample for a particular tissue and mRNA from the normal adjacent sample for that same tissue from the same individual. Of the normal samples 6 were blood samples which measured the expression levels in blood cells. Additionally, 2 prostatitis, and 4 Benign Prostatic Hyperplasia (BPH) samples are included. All the values are compared to cancer pool reference HUMREF00HR (calibrator).

The table below contains the relative expression level values for the sample as compared to the calibrator. The table includes the Sample ID, and expression level values for the following samples: Cancer (CAN), Normal Adjacent Tissue (NAT), Normal Tissue (NRM), Benign Prostatic Hyperplasia (BPH), and Prostatitis (PROST).

Sample ID	CAN	NAT	NRM	BPH	PROST
OVRA084	0.46	0.17			
OVRG010	1.55	3.95			
OVRG021	6.74	6.08			
OVR1157	4.90				
OVR773O	8.80				
OVR814O	3.90				
OVRC360	1.37				
OVR1005O	19.92				
OVR1040O	20.35				
OVR105O	5.63				

OVR130X	19.60				
OVR718O	55.03				
OVRA1B	34.34				
OVR247A			1.35		
OVR35GA			2.50		
OVRC087			0.98		
OVRC109			0.23		
OVR206I			3.37		
OVR515O			1.42		
OVR18GA			1.49		
OVR337O			3.54		
OVR123O			3.29		
OVRC177			3.49		
OVR40G			1.62		
OVRC004			9.36		
BLD030B	3.36	0.72			
BLD520B	3.23	2.25			
BLDTR17	1.08	1.89			
CLN401C	3.90	3.01			
CLNAS43	4.55	1.92			
CLNAS98	3.44	2.33			
CLNCM12	3.07	3.22			
CLNDC19	7.72	2.05			
CLNRC01	1.80	2.17			
CLNRS53	2.59	3.02			
CLNSG27	2.69	4.49			
CLNTX01	5.68	5.10			
CVXKS52	9.10	10.59			
CVXNK23	9.81	41.11			
CVXNKS54	20.97	12.22			
CVXNKS55	37.01	21.89			
CVXNKS81	17.75	35.18			
ENDO10479	13.27	1.33			
ENDO28XA	13.53	4.98			
ENDO8XA	0.34	0.58			
KID106XD	0.28	0.70			
KID107XD	5.01	2.27			
KID109XD	7.16	4.83			
KID10XD	1.34	0.46			
KID22K	2.79	0.65			
LNG205L	1.40	4.10			
LNG315L	8.68	8.32			
LNG507L	6.50	4.85			
LNG528L	9.26	4.03			
LNG8837L	4.36	5.37			
LNGAC11	2.50	4.70			
LNGAC39	16.03	4.63			

LNGSQ80	3.70	0.84			
LNGSQ81	14.10	7.33			
LVR15XA	0.05	0.03			
LVR174L	0.15	0.12			
LVR187L	0.00	9.89			
MAM19DN	17.32	17.15			
MAM42DN	15.00	9.52			
MAM517	66.52	6.34			
MAM781M	4.45	3.02			
MAM869M	9.21	1.73			
MAM976M	28.64	3.82			
MAMS570	22.00	25.62			
MAMS699	5.42	5.54			
MAMS997	10.63	7.95			
PAN71XL	5.56	5.74			
PAN82XP	2.41	26.35			
PAN92X	52.91	6.82			
PRO23B	7.13	7.97			
PRO65XB	5.61	6.99			
PRO675P	7.00	4.30			
PRO84XB	7.18	6.80			
PRO958P	6.32	4.35			
PRO263C				6.28	
PRO276P				4.78	
PRO767B				10.75	
PRO855P				5.51	
PRO10R					9.97
PRO20R					8.32
SKN287S	6.30	6.42			
SKN39A	4.04	1.83			
SKN669S	6.16	19.67			
SMINT171S	11.57	8.96			
SMINT20SM	10.72	4.23			
SMINTH89	5.77	4.77			
STO261S	8.85	2.39			
STO288S	2.33	1.18			
STO509L	5.78	10.86			
STO88S	4.07	1.01			
THRD143N	8.25	15.21			
THRD270T	10.97	7.35			
THRD56T	9.88	11.23			
TST39X	9.41	4.59			
TST647T	11.31	1.05			
TST663T	7.35	2.94			
UTR135XO	2.34	5.62			
UTR85XU	17.13	6.68			
BLOB1			7.23		

BLOB3			3.50		
BLOB5			122.49		
BLOB6			9.34		
BLOB11			5.44		
BLO982B			14.78		
ADR48AD			0.61		
BRN10BR			0.99		
CLN01CL			0.51		
CVX1ACV			14.89		
ESO01ES			5.63		
HRT46HR			0.00		
HUMREF00HR	1.00				
KID55KD			0.29		
LVR89LV			0.05		
LNG90LN			2.25		
MAM01MA			1.00		
MSL84MU			0.00		
OVR3APV			0.93		
PAN04PA			2.42		
PLA59PL			3.63		
PRO09PR			3.03		
REC21RC			2.74		
SMINT59SM			2.21		
SPL7GSP			1.19		
STO09ST			0.87		
THYM99TM			5.68		
TRA16TR			8.67		
TST4GTS			9.06		
UTR57UT			1.93		

0.00= Negative or Not Detected

The sensitivity for Ovr218 expression was calculated for the cancer samples versus normal samples. The sensitivity value indicates the percentage of cancer samples that show levels of Ovr218 at least 2 fold higher than the normal tissue or the corresponding normal adjacent form the same patient.

This specificity is an indication of the level of ovary tissue specific expression of the transcript compared to all the other tissue types tested in our assay. Thus, these experiments indicate Ovr218 being useful as an ovarian cancer diagnostic marker and/or therapeutic target.

Sensitivity and specificity data is reported in the table below.

	CLN	LNG	MAM	OVR	PRO
Sensitivity, Up vs. NAT	22%	33%	33%	0%	0%

Sensitivity, Down vs. NAT	0%	11%	0%	0%	0%
Sensitivity, Up vs. NRM	100%	56%	100%	77%	80%
Sensitivity, Down vs. NRM	0%	0%	0%	8%	0%
Specificity	6.88 %	9.52 %	20.63 %	8.94 %	9.95 %

Altogether, the tissue specificity, plus the mRNA differential expression in the samples tested are believed to make Ovr218 a good marker for diagnosing, monitoring, staging, imaging and/or treating ovarian cancer.

Additionally, the tissue specificity, plus the mRNA differential expression in the samples tested may make Ovr218 a good marker for diagnosing, monitoring, staging, imaging and/or treating breast cancer.

Primers used for QPCR Expression Analysis of Ovr218 are as follows:

(Ovr218_forward): TGCCCAGCTGTGGTTTACATTA (SEQ ID NO:314)

(Ovr218_reverse): CACCACCTCGCCATTCTCA (SEQ ID NO:315)

(Ovr218_probe): TTCACTGTGAACATCATCTTGGCA (SEQ ID NO:316)

DEX0455_049.nt.1 (Ovr232)

The relative expression level of Ovr232 in various tissue samples is included below. Tissue samples include 73 pairs of matching samples, 10 non matched cancer samples, and 36 normal samples, all from various tissues annotated in the table. A matching pair is formed by mRNA from the cancer sample for a particular tissue and mRNA from the normal adjacent sample for that same tissue from the same individual. Of the normal samples 4 were blood samples which measured the expression levels in blood cells. Additionally, 2 prostatitis, and 4 Benign Prostatic Hyperplasia (BPH) samples are included. All the values are compared to ovarian cancer sample OVRAO84 (calibrator).

The table below contains the relative expression level values for the sample as compared to the calibrator. The table includes the Sample ID, and expression level values for the following samples: Cancer (CAN), Normal Adjacent Tissue (NAT), Normal Tissue (NRM), Benign Prostatic Hyperplasia (BPH), and Prostatitis (PROST).

Sample ID	CAN	NAT	NRM	BPH	PROST
OVRA084	1.00	0.10			
OVRG010	0.01	0.31			
OVRG021	0.39	0.02			
OVR1157	2.79				

OVR773O	1.14				
OVR814O	0.37				
OVRC360	0.00				
OVR1005O	5.91				
OVR1040O	5.77				
OVR105O	1.68				
OVR130X	1.08				
OVR718O	0.55				
OVRA1B	4.48				
OVR247A			0.00		
OVR35GA			0.00		
OVRC087			0.00		
OVRC109			0.00		
OVR206I			0.03		
OVR515O			0.00		
OVR18GA			0.00		
OVR123O			0.00		
OVRC177			0.02		
OVR40G			0.00		
OVRC004			0.00		
BLD030B	0.26	0.00			
BLD520B	0.13	0.02			
BLDTR17	0.24	0.25			
CLN401C	3.46	2.62			
CLNAS43	4.08	1.49			
CLNAS98	1.19	5.27			
CLNCM12	2.46	7.45			
CLNDC19	9.09	1.85			
CLNRC01	2.55	3.52			
CLNRS53	1.38	9.36			
CLNSG27	4.28	3.65			
CLNTX01	3.83	4.54			
CVXKS52	0.15	0.12			
CVXNK23	0.13	0.00			
CVXNKS54	0.59	0.54			
CVXNKS55	0.58	0.15			
CVXNKS81	0.25	0.61			
ENDO10479	6.19	1.01			
ENDO28XA	6.03	0.82			
ENDO8XA	0.40	1.67			
KID106XD	0.02	0.24			
KID107XD	0.10	0.34			
KID109XD	0.07	0.59			
KID10XD	0.00	0.15			
KID22K	0.05	0.14			
LNG205L	0.08	1.91			
LNG315L	1.42	0.43			

LNG507L	0.96	0.87			
LNG528L	9.39	0.92			
LNG8837L	1.08	0.45			
LNGAC11	0.28	1.23			
LNGAC39	13.19	0.76			
LNGSQ80	2.02	0.86			
LNGSQ81	2.19	0.67			
LVR15XA	0.00	0.01			
LVR174L	0.00	0.01			
LVR187L	0.00	10.06			
MAM19DN	0.46	0.85			
MAM42DN	0.71	0.74			
MAM517	3.27	0.33			
MAM781M	1.52	0.34			
MAM976M	0.83	0.37			
MAMS570	0.35	1.02			
MAMS699	0.28	0.39			
MAMS997	1.23	0.52			
PAN71XL	6.96	4.45			
PAN82XP	0.15	2.74			
PAN92X	2.89	0.00			
PRO23B	0.23	0.12			
PRO65XB	0.24	0.50			
PRO675P	0.40	0.21			
PRO84XB	0.45	0.30			
PRO958P	0.22	0.21			
PRO263C				0.27	
PRO276P				0.12	
PRO767B				0.24	
PRO855P				0.21	
PRO10R					0.18
PRO20R					0.44
SKN287S	0.38	0.11			
SKN39A	0.00	0.00			
SKN669S	0.03	0.08			
SMINT171S	3.18	4.30			
SMINT20SM	8.08	5.63			
SMINTH89	8.24	3.50			
STO261S	6.10	2.42			
STO288S	5.52	0.23			
STO88S	2.64	0.14			
THRD143N	1.00	5.56			
THRD270T	8.64	11.30			
THRD56T	3.91	1.96			
TST39X	0.42	0.56			
TST647T	4.38	0.11			
TST663T	2.81	0.13			

UTR135XO	0.40	0.48			
UTR85XU	3.06	1.79			
BLOB3			0.31		
BLOB6			0.00		
BLOB11			0.00		
BLO982B			0.00		
ADR48AD			0.00		
BRN10BR			0.07		
CLN01CL			0.57		
ESO01ES			0.00		
HUMREF00HR	0.17				
KID55KD			0.05		
LVR89LV			0.00		
LNG90LN			2.56		
MAM01MA			0.13		
MSL84MU			0.00		
OVR3APV			0.00		
PAN04PA			0.09		
PLA59PL			0.00		
PRO09PR			0.30		
REC21RC			4.27		
SMINT59SM			0.97		
SPL7GSP			0.03		
STO09ST			0.09		
THYM99TM			0.04		
TRA16TR			0.43		
TST4GTS			0.11		
UTR57UT			0.07		

0.00= Negative or Not Detected

The sensitivity for Ovr232 expression was calculated for the cancer samples versus normal samples. The sensitivity value indicates the percentage of cancer samples that show levels of Ovr232 at least 2 fold higher than the normal tissue or the corresponding normal adjacent form the same patient.

This specificity is an indication of the level of ovary tissue specific expression of the transcript compared to all the other tissue types tested in our assay. Thus, these experiments indicate Ovr232 being useful as an ovarian cancer diagnostic marker and/or therapeutic target.

Sensitivity and specificity data is reported in the table below.

	CLN	LNG	MAM	OVR	PRO
Sensitivity, Up vs. NAT	22%	67%	44%	0%	0%
Sensitivity, Down vs. NAT	33%	22%	11%	0%	20%

Sensitivity, Up vs. NRM	100%	22%	100%	92%	0%
Sensitivity, Down vs. NRM	0%	44%	0%	8%	0%
Specificity	50.82 %	33.88 %	22.95 %	21.84 %	19.46 %

Altogether, the tissue specificity, plus the mRNA differential expression in the samples tested are believed to make Ovr232 a good marker for diagnosing, monitoring, staging, imaging and/or treating ovarian cancer.

Primers used for QPCR Expression Analysis of Ovr232 are as follows:

(Ovr232_forward): GCTCAAAGCGTGAGTAAAATATCCT (SEQ ID NO:317)

(Ovr232_reverse): CCACACTTACTTTGTAACATGATTCAGA (SEQ ID NO:318)

(Ovr232_probe): TTTGACTTAATACTTCTTTAATTGATGTGCCTTGAGTTGG (SEQ ID NO:319)

DEX0455_049.nt.2 (Ovr232v1)

The relative expression level of Ovr232v1 in various tissue samples is included below. Tissue samples include 75 pairs of matching samples, 10 non matched cancer samples, and 40 normal samples, all from various tissues annotated in the table. A matching pair is formed by mRNA from the cancer sample for a particular tissue and mRNA from the normal adjacent sample for that same tissue from the same individual. Of the normal samples 5 were blood samples which measured the expression levels in blood cells. Additionally, 2 prostatitis, and 4 Benign Prostatic Hyperplasia (BPH) samples are included. All the values are compared to normal colon sample CLN01CL (calibrator).

The table below contains the relative expression level values for the sample as compared to the calibrator. The table includes the Sample ID, and expression level values for the following samples: Cancer (CAN), Normal Adjacent Tissue (NAT), Normal Tissue (NRM), Benign Prostatic Hyperplasia (BPH), and Prostatitis (PROST).

Sample ID	CAN	NAT	NRM	BPH	PROST
OVRA084	0.02	0.67			
OVRG010	0.00	0.00			
OVRG021	0.10	0.00			
OVR1157	0.00				
OVR7730	0.00				
OVR988Z	0.00				
OVRC360	0.00				

OVR1005O	0.42				
OVR1040O	0.53				
OVR105O	0.09				
OVR130X	0.53				
OVR718O	0.25				
OVRA1B	0.26				
OVR247A			0.00		
OVR35GA			0.05		
OVRC087			0.00		
OVRC109			0.00		
OVR206I			0.00		
OVR515O			0.00		
OVR18GA			0.00		
OVR337O			0.00		
OVR123O			0.38		
OVRC177			0.01		
OVR40G			0.00		
OVR451O			0.00		
BLD030B	0.06	0.09			
BLD520B	0.20	0.03			
BLDTR17	0.46	0.01			
CLN401C	0.18	0.22			
CLNAS43	0.39	0.21			
CLNAS98	0.31	0.47			
CLNCM12	0.10	0.20			
CLNDC19	0.40	0.07			
CLNRC01	0.27	0.13			
CLNRS53	0.15	0.33			
CLNSG27	0.17	0.25			
CLNTX01	0.13	0.20			
CVXKS52	0.00	0.00			
CVXNKS55	0.00	0.12			
CVXNKS25	0.85	0.00			
CVXNKS18	0.00	0.00			
CVXNKS54	0.00	0.00			
ENDO10479	0.13	0.00			
ENDO28XA	0.32	0.12			
ENDO8XA	0.07	0.40			
KID106XD	0.05	0.10			
KID12XD	0.04	0.12			
KID10XD	0.05	0.05			
KID22K	0.02	0.03			
KID107XD	0.00	0.04			
LNG205L	0.00	0.26			
LNG315L	0.38	0.00			
LNG507L	0.20	0.00			
LNG528L	0.37	0.37			

LNG8837L	0.10	0.06			
LNGAC11	0.03	0.06			
LNGAC39	0.58	0.63			
LNGSQ80	0.21	0.19			
LNGSQ81	0.15	0.00			
LVR15XA	0.00	0.00			
LVR174L	0.00	0.00			
LVR187L	0.00	0.37			
MAM19DN	0.12	0.25			
MAM42DN	0.44	0.64			
MAM517	0.25	0.00			
MAM781M	0.24	0.67			
MAM869M	0.04	0.00			
MAM976M	0.22	0.00			
MAMS570	0.00	0.47			
MAMS699	0.00	0.00			
MAMS997	0.11	0.04			
PAN71XL	1.10	0.31			
PAN77X	0.00	0.00			
PAN92X	0.19	0.00			
PRO10R					0.00
PRO20R					0.20
PRO23B	0.17	0.10			
PRO263C				0.54	
PRO276P				0.27	
PRO65XB	0.17	0.11			
PRO675P	0.47	0.85			
PRO767B				0.10	
PRO84XB	0.12	0.13			
PRO855P				0.08	
PRO958P	0.15	0.12			
SKN287S	0.10	0.00			
SKN39A	0.06	0.00			
SKN669S	0.00	0.51			
SMINT171S	0.38	0.67			
SMINT20SM	0.23	0.40			
SMINTH89	0.14	0.31			
STO261S	0.69	0.24			
STO288S	0.36	0.17			
STOAC93	0.00	0.00			
STO88S	0.00	0.17			
THRD143N	0.15	0.25			
THRD270T	0.37	0.28			
THRD56T	0.34	0.45			
TST39X	0.20	0.43			
TST647T	0.59	0.41			
TST663T	0.33	0.25			

UTR135XO	0.19	0.13			
UTR85XU	1.42	0.14			
BLOB3			0.00		
BLOB11			0.00		
BLO69			0.00		
BLO72			0.00		
BLO73			0.00		
ADR48AD			0.00		
BRN10BR			0.00		
CLN01CL			0.12		
CVX06CV			0.00		
ESO01ES			0.00		
HRT46HR			0.00		
HUMREF00HR	0.08				
KID55KD			0.02		
LVR89LV			0.00		
LNG90LN			1.00		
MAM01MA			0.10		
MSL84MU			0.00		
OVR3APV			0.03		
PAN04PA			0.17		
PLA59PL			0.00		
PRO09PR			0.00		
REC21RC			0.36		
SMINT59SM			0.13		
SPL7GSP			0.09		
STO09ST			0.39		
THYM99TM			0.00		
TRA16TR			0.09		
TST4GTS			0.50		
UTR57UT			0.15		

0.00= Negative or Not Detected

The sensitivity for Ovr232v1 expression was calculated for the cancer samples versus normal samples. The sensitivity value indicates the percentage of cancer samples that show levels of Ovr232v1 at least 2 fold higher than the normal tissue or the corresponding normal adjacent form the same patient.

This specificity is an indication of the level of ovary tissue specific expression of the transcript compared to all the other tissue types tested in our assay. Thus, these experiments indicate Ovr232v1 being useful as an ovarian cancer diagnostic marker and/or therapeutic target.

Sensitivity and specificity data is reported in the table below.

	CLN	LNG	MAM	OVR	PRO

Sensitivity, Up vs. NAT	22%	33%	44%	0%	0%
Sensitivity, Down vs. NAT	22%	22%	33%	0%	0%
Sensitivity, Up vs. NRM	44%	0%	44%	62%	100%
Sensitivity, Down vs. NRM	0%	89%	33%	0%	0%
Specificity	36.7 %	34.57 %	32.45 %	28.65 %	35.26 %

Altogether, the tissue specificity, plus the mRNA differential expression in the samples tested are believed to make Ovr232v1 a good marker for diagnosing, monitoring, staging, imaging and/or treating ovarian cancer.

Primers used for QPCR Expression Analysis of Ovr232v1 are as follows:

(Ovr232v1_forward): GGCGGTGACTCATCAACGA (SEQ ID NO:320)

(Ovr232v1_reverse): CATTGACGATTATTATTCACAAAGCA (SEQ ID NO:321)

(Ovr232v1_probe): GCGGCCAGAGAATGTGTCTGTGAAAACT (SEQ ID NO:322)

DEX0455_049.nt.3 (Ovr232v2)

The relative expression level of Ovr232v2 in various tissue samples is included below. Tissue samples include 72 pairs of matching samples, 12 non matched cancer samples, and 37 normal samples, all from various tissues annotated in the table. A matching pair is formed by mRNA from the cancer sample for a particular tissue and mRNA from the normal adjacent sample for that same tissue from the same individual. Of the normal samples 5 were blood samples which measured the expression levels in blood cells. Additionally, 2 prostatitis, and 4 Benign Prostatic Hyperplasia (BPH) samples are included. All the values are compared to normal spleen sample SPL7GSP (calibrator).

The table below contains the relative expression level values for the sample as compared to the calibrator. The table includes the Sample ID, and expression level values for the following samples: Cancer (CAN), Normal Adjacent Tissue (NAT), Normal Tissue (NRM), Benign Prostatic Hyperplasia (BPH), and Prostatitis (PROST).

Sample ID	CAN	NAT	NRM	BPH	PROST
OVRA084	20.82	1.47			
OVRG010	7.06	0.00			
OVRG021	2.01	0.55			
OVR1157	17.09				

OVR773O	31.56				
OVR988Z	17.68				
OVRC360	0.00				
OVR1005O	20.28				
OVR1040O	29.36				
OVR105O	15.24				
OVR130X	10.08				
OVR718O	12.73				
OVRA1B	34.60				
OVR247A			0.00		
OVR35GA			0.11		
OVRC087			0.00		
OVRC109			0.00		
OVR206I			0.43		
OVR515O			1.11		
OVR18GA			0.00		
OVR123O			3.47		
OVRC177			0.08		
OVR40G			0.06		
BLD030B	6.81	0.00			
BLD520B	4.04	0.57			
BLDTR17	3.89	2.17			
CLN401C	22.89	17.80			
CLNAS43	72.65	16.04			
CLNAS98	15.32	35.15			
CLNCM12	17.48	29.75			
CLNDC19	81.83	20.01			
CLNRC01	20.30	18.70			
CLNRS53	17.98	55.34			
CLNSG27	59.40	41.80			
CLNTX01	30.45	37.83			
CVXKS52	3.47	2.77			
CVXNKS55	12.43	2.43			
CVXNKS18	0.00	0.54			
CVXNKS54	13.64	2.13			
ENDO10479	95.97	4.22			
ENDO28XA	39.72	8.50			
ENDO8XA	3.02	11.79			
KID106XD	0.18	1.97			
KID12XD	1.46	10.05			
KID10XD	0.35	1.92			
KID22K	0.65	1.57			
KID107XD	4.13	2.74			
LNG205L	3.09	13.46			
LNG315L	18.48	9.39			
LNG507L	15.67	4.96			
LNG528L	78.28	10.67			

LNG8837L	14.25	6.13			
LNGAC11	7.45	16.04			
LNGAC39	151.52	5.87			
LNGSQ80	27.78	24.91			
LNGSQ81	9.10	5.92			
LVR15XA	0.27	0.09			
LVR174L	0.00	0.23			
LVR187L	0.00	85.59			
MAM19DN	7.21	18.30			
MAM42DN	29.31	5.38			
MAM517	13.24	1.54			
MAM781M	26.05	0.95			
MAM869M	4.02	0.00			
MAM976M	13.42	2.33			
MAMS570	4.31	5.78			
MAMS699	1.12	4.34			
MAMS997	13.01	5.21			
PAN71XL	64.87	58.75			
PAN77X	0.00	0.00			
PAN92X	26.90	0.00			
PRO10R					2.57
PRO20R					5.10
PRO23B	3.74	3.66			
PRO263C				3.92	
PRO276P				1.99	
PRO65XB	3.35	4.51			
PRO675P	8.17	1.15			
PRO767B				10.45	
PRO84XB	5.75	3.97			
PRO855P				3.29	
PRO958P	2.91	5.35			
SKN287S	5.73	0.91			
SKN39A	0.00				
SKN669S	0.13	2.14			
SMINT171S	56.03	62.72			
SMINT20SM	106.47	33.80			
SMINTH89	96.97	40.02			
STO261S	118.64	19.05			
STO288S	47.55	4.07			
STOAC93	67.18	64.23			
STO88S	79.32				
THRD143N	14.71	30.26			
THRD270T	43.65	40.86			
THRD56T	23.82	8.72			
TST39X	6.89	5.65			
TST647T	30.28	3.55			
TST663T	23.55	1.69			

UTR135XO	2.75	5.63			
UTR85XU	32.07	28.53			
BLOB3			2.60		
BLOB11			0.00		
BLO69			0.00		
BLO72			0.34		
BLO73			0.00		
ADR48AD			0.00		
BRN10BR			0.47		
CLN01CL			24.82		
ESO01ES			0.00		
HRT46HR			0.00		
HUMREF00HR	4.31				
KID55KD			2.28		
LVR89LV			0.02		
LNG90LN			10.08		
MAM01MA			1.17		
MSL84MU			0.00		
OVR3APV			0.02		
PAN04PA			0.61		
PLA59PL			0.00		
PRO09PR			8.47		
REC21RC			95.94		
SMINT59SM			16.37		
SPL7GSP			1.00		
STO09ST			2.19		
THYM99TM			0.83		
TRA16TR			6.78		
TST4GTS			1.57		
UTR57UT			2.24		

0.00= Negative or Not Detcted

The sensitivity for Ovr232v2 expression was calculated for the cancer samples versus normal samples. The sensitivity value indicates the percentage of cancer samples that show levels of Ovr232v2 at least 2 fold higher than the normal tissue or the corresponding normal adjacent form the same patient.

This specificity is an indication of the level of ovary tissue specific expression of the transcript compared to all the other tissue types tested in our assay. Thus, these experiments indicate Ovr232v2 being useful as an ovarian cancer diagnostic marker and/or therapeutic target.

Sensitivity and specificity data is reported in the table below.

	CLN	LNG	MAM	OVR	PRO
Sensitivity, Up vs. NAT	22%	44%	67%	0%	20%

Sensitivity, Down vs. NAT	22%	22%	22%	0%	0%
Sensitivity, Up vs. NRM	33%	33%	89%	92%	0%
Sensitivity, Down vs. NRM	0%	11%	0%	8%	60%
Specificity	36.46 %	29.28 %	25.41 %	24.28 %	19.13 %

Altogether, the tissue specificity, plus the mRNA differential expression in the samples tested are believed to make Ovr232v2 a good marker for diagnosing, monitoring, staging, imaging and/or treating ovarian cancer.

Primers used for QPCR Expression Analysis of Ovr232v2 are as follows:

(Ovr232v2_forward): CCTTTTTATCCACTTACAGATCAACCA (SEQ ID NO:323)

(Ovr232v2_reverse): ACAAGCAAGATGCATGTGAGTGA (SEQ ID NO:324)

(Ovr232v2_probe): ATGGTTCGCTGCTGCCGTT (SEQ ID NO:325)

DEX0455_049.nt.4 (Ovr232v3)

The relative expression level of Ovr232v3 in various tissue samples is included below. Tissue samples include 75 pairs of matching samples, 10 non matched cancer samples, and 39 normal samples, all from various tissues annotated in the table. A matching pair is formed by mRNA from the cancer sample for a particular tissue and mRNA from the normal adjacent sample for that same tissue from the same individual. Of the normal samples 5 were blood samples which measured the expression levels in blood cells. Additionally, 2 prostatitis, and 4 Benign Prostatic Hyperplasia (BPH) samples are included. All the values are compared to normal lung sample LNG90LN (calibrator).

The table below contains the relative expression level values for the sample as compared to the calibrator. The table includes the Sample ID, and expression level values for the following samples: Cancer (CAN), Normal Adjacent Tissue (NAT), Normal Tissue (NRM), Benign Prostatic Hyperplasia (BPH), and Prostatitis (PROST).

Sample ID	CAN	NAT	NRM	BPH	PROST
OVRA084	0.00	0.00			
OVRG010	0.07	0.00			
OVRG021	0.00	0.00			
OVR1157	0.01				
OVR773O	0.00				
OVR988Z	0.00				
OVRC360	0.00				
OVR1005O	0.52				

OVR1040O	0.55				
OVR105O	0.25				
OVR130X	0.00				
OVR718O	0.29				
OVRA1B	0.22				
OVR247A			0.00		
OVRC087			0.00		
OVRC109			0.00		
OVR206I			0.00		
OVR515O			0.00		
OVR18GA			0.00		
OVR337O			0.00		
OVR123O			0.00		
OVRC177			0.00		
OVR40G			0.00		
OVR451O			0.00		
BLD030B	0.12	0.00			
BLD520B	0.00	0.00			
BLDTR17	0.00	0.02			
CLN401C	0.57	0.24			
CLNAS43	1.60	0.00			
CLNAS98	0.86	0.00			
CLNCM12	0.06	0.06			
CLNDC19	0.47	0.03			
CLNRC01	0.12	0.12			
CLNRS53	0.00	0.00			
CLNSG27	1.08	0.00			
CLNTX01	0.00	0.41			
CVXKS52	0.00	0.00			
CVXNKS55	0.00	0.00			
CVXNKS25	0.00	0.00			
CVXNKS18	0.00	0.00			
CVXNKS54	0.00	0.00			
ENDO10479	0.30	0.00			
ENDO28XA	0.19	0.00			
ENDO8XA	0.00	0.46			
KID106XD	0.00	0.00			
KID12XD	0.00	0.00			
KID10XD	0.00	0.04			
KID22K	0.00	0.02			
KID107XD	0.00	0.12			
LNG205L	0.00	0.68			
LNG315L	0.00	0.00			
LNG507L	0.00	0.00			
LNG528L	1.50	0.00			
LNG8837L	0.96	0.81			
LNGAC11	0.03	0.00			

LNGAC39	0.35	1.20			
LNGSQ80	0.87	0.00			
LNGSQ81	0.65	0.00			
LVR15XA	0.10	0.00			
LVR174L	0.00	0.00			
LVR187L	0.00	0.38			
MAM19DN	0.00	0.00			
MAM42DN	0.00	0.07			
MAM517	0.00	0.00			
MAM781M	0.00	0.00			
MAM869M	0.00	0.00			
MAM976M	0.00	0.00			
MAMS570	0.00	0.00			
MAMS699	0.00	0.00			
MAMS997	0.05	0.21			
PAN71XL	0.00	0.64			
PAN77X	0.00	0.00			
PAN92X	0.19	0.00			
PRO10R					0.00
PRO20R					0.00
PRO23B	0.04	0.00			
PRO263C				0.00	
PRO276P				0.00	
PRO65XB	0.09	0.00			
PRO675P	0.68	0.00			
PRO767B				0.09	
PRO84XB	0.00	0.00			
PRO855P				0.01	
PRO958P	0.00	0.00			
SKN287S	0.06	0.00			
SKN39A	0.00	0.00			
SKN669S	0.00	0.00			
SMINT171S	0.03	0.00			
SMINT20SM	0.55	0.24			
SMINTH89	0.00	0.47			
STO261S	1.03	0.00			
STO288S	0.54	0.00			
STOAC93	0.00	2.29			
STO88S	0.00	0.00			
THRD143N	0.51	2.00			
THRD270T	0.49	0.97			
THRD56T	0.79	0.00			
TST39X	0.00	0.00			
TST647T	0.52	0.59			
TST663T	0.40	0.46			
UTR135XO	0.00	0.00			
UTR85XU	0.77	0.29			

BLOB3			0.00		
BLOB11			0.00		
BLO69			0.00		
BLO72			0.00		
BLO73			0.00		
ADR48AD			0.00		
BRN10BR			0.00		
CLN01CL			0.03		
CVX06CV			0.00		
ESO01ES			0.00		
HRT46HR			0.00		
HUMREF00HR	0.00				
KID55KD			0.01		
LVR89LV			0.00		
LNG90LN			1.00		
MAM01MA			0.06		
MSL84MU			0.00		
OVR3APV			0.01		
PAN04PA			0.00		
PLA59PL			0.00		
PRO09PR			0.00		
REC21RC			1.27		
SMINT59SM			0.00		
SPL7GSP			0.00		
STO09ST			0.00		
THYM99TM			0.00		
TRA16TR			0.00		
TST4GTS			1.21		
UTR57UT			0.00		

0.00= Negative or Not Detected

The sensitivity for Ovr232v3 expression was calculated for the cancer samples versus normal samples. The sensitivity value indicates the percentage of cancer samples that show levels of Ovr232v3 at least 2 fold higher than the normal tissue or the corresponding normal adjacent form the same patient.

This specificity is an indication of the level of ovary tissue specific expression of the transcript compared to all the other tissue types tested in our assay. Thus, these experiments indicate Ovr232v3 being useful as an ovarian cancer diagnostic marker and/or therapeutic target.

Sensitivity and specificity data is reported in the table below.

	CLN	LNG	MAM	OVR	PRO
Sensitivity, Up vs. NAT	56%	44%	0%	0%	60%

Sensitivity, Down vs. NAT	11%	22%	22%	0%	0%
Sensitivity, Up vs. NRM	78%	0%	0%	62%	60%
Sensitivity, Down vs. NRM	22%	56%	89%	0%	0%
Specificity	72.73 %	70.59 %	61.5 %	62.36 %	63.49 %

Altogether, the tissue specificity, plus the mRNA differential expression in the samples tested are believed to make Ovr232v3 a good marker for diagnosing, monitoring, staging, imaging and/or treating ovarian cancer.

Primers used for QPCR Expression Analysis of Ovr232v3 are as follows:

(Ovr232v3_forward): CCTCACTTCGCAGCTTTGCT (SEQ ID NO:326)

(Ovr232v3_reverse): CTGGCATTGACGATTATTATTCACA (SEQ ID NO:327)

(Ovr232v3_probe): CTGTGAAAACTACAAGCTGGCCGTAAACTGCT (SEQ ID NO:328)

DEX0455_052.nt.2 (Ovr107v1)

The relative expression level of Ovr107v1 in various tissue samples is included below. Tissue samples include 69 pairs of matching samples, 14 non matched cancer samples, and 33 normal samples, all from various tissues annotated in the table. A matching pair is formed by mRNA from the cancer sample for a particular tissue and mRNA from the normal adjacent sample for that same tissue from the same individual. Of the normal samples 2 were blood samples which measured the expression levels in blood cells. Additionally, 2 prostatitis, and 4 Benign Prostatic Hyperplasia (BPH) samples are included. All the values are compared to prostate normal sample PRO09PR (calibrator).

The table below contains the relative expression level values for the sample as compared to the calibrator. The table includes the Sample ID, and expression level values for the following samples: Cancer (CAN), Normal Adjacent Tissue (NAT), Normal Tissue (NRM), Benign Prostatic Hyperplasia (BPH), and Prostatitis (PROST).

Sample ID	CAN	NAT	NRM	BPH	PROST
OVRA084	1.11	0.00			
OVRG010	0.00	6.59			
OVRG021	0.36	0.35			
OVR1157	3.79				
OVR7730	7.68				
OVR8140	1.90				
OVRC360	0.00				

OVR1005O	4.09				
OVR1040O	3.29				
OVR105O	4.05				
OVR130X	0.00				
OVR718O	0.84				
OVRA1B	3.99				
OVR247A			0.12		
OVR35GA			0.14		
OVRC087			0.06		
OVRC109			0.22		
OVR206I			0.42		
OVR515O			0.00		
OVR18GA			0.00		
OVRC177			0.02		
OVR40G			0.00		
BLD030B	0.79	0.00			
BLD520B	0.10	0.12			
BLDTR17	2.53	1.19			
CLN401C	0.26	0.44			
CLNAS43	4.02	1.01			
CLNAS98	1.42	0.50			
CLNCM12	1.48	0.45			
CLNDC19	2.32	0.79			
CLNRC01	0.33	0.15			
CLNRS53	0.31	0.88			
CLNSG27	2.00	1.15			
CLNTX01	0.00	0.00			
CVXKS52	1.77	3.80			
CVXNK23	1.76				
CVXNKS54	2.77	3.22			
CVXNKS55	6.45	9.73			
CVXNKS81	2.00				
ENDO10479	5.01	1.45			
ENDO28XA	5.66	0.29			
ENDO8XA	0.85	0.18			
KID106XD	0.00	0.61			
KID107XD	0.44	1.12			
KID109XD	2.85	0.99			
KID10XD	0.00	0.09			
KID22K	0.32	0.03			
LNG205L	0.26	1.68			
LNG315L	0.44	0.44			
LNG507L	0.24	0.00			
LNG528L	0.19	0.17			
LNG8837L	1.07	0.62			
LNGAC11	0.63	0.30			
LNGAC39	1.29	1.24			

LNGSQ80	1.39	0.25			
LNGSQ81	1.23	0.56			
LVR15XA	0.00	0.04			
LVR174L	0.00	0.02			
LVR187L	0.25	0.86			
MAM19DN	1.91	1.04			
MAM42DN	0.36	0.00			
MAM517		0.00			
MAM781M	0.00	0.53			
MAM869M	1.40	1.23			
MAM976M	2.55	0.00			
MAMS570	0.00	1.69			
MAMS699	1.35	0.00			
MAMS997	2.41	1.23			
PAN71XL	0.72	0.00			
PAN82XP	0.71				
PAN92X	5.33				
PRO23B	1.06	0.93			
PRO65XB	0.61	0.70			
PRO675P	0.57	0.48			
PRO84XB	0.62	0.75			
PRO958P	1.10	1.03			
PRO263C				1.38	
PRO276P				0.66	
PRO767B				2.26	
PRO855P				0.76	
PRO10R					0.26
PRO20R					0.36
SKN287S	2.27	0.00			
SKN39A	0.54	0.00			
SKN669S	0.52	6.42			
SMINT171S	1.91	0.09			
SMINT20SM	3.08	1.13			
SMINTH89	1.92	1.28			
STO261S	1.20	0.35			
STO288S	0.14	0.29			
STO88S	0.58	0.00			
THRD143N	1.09	6.12			
THRD270T	5.60	6.15			
THRD56T	2.63	2.16			
TST39X	0.58	0.29			
TST647T	0.41	0.03			
TST663T	0.95	0.07			
UTR135XO	0.63	1.00			
UTR85XU	0.00	0.19			
BLOB3			0.35		
BLOB11			0.00		

ADR48AD			0.00		
BRN10BR			0.00		
CLN01CL			0.79		
ESO01ES			1.69		
HRT46HR			0.00		
HUMREF00HR	0.67				
KID55KD			0.17		
LVR89LV			0.00		
LNG90LN			0.36		
MAM01MA			0.55		
MSL84MU			0.00		
OVR3APV			0.33		
PAN04PA			0.24		
PLA59PL			5.67		
PRO09PR			1.00		
REC21RC			0.51		
SMINT59SM			0.12		
SPL7GSP			0.08		
STO09ST			2.33		
THYM99TM			0.20		
TRA16TR			2.37		
TST4GTS			0.33		
UTR57UT			0.32		

Note: 0.00= Negative or Not Detected

The sensitivity for Ovr107v1 expression was calculated for the cancer samples versus normal samples. The sensitivity value indicates the percentage of cancer samples that show levels of Ovr107v1 at least 2 fold higher than the normal tissue or the corresponding normal adjacent form the same patient.

This specificity is an indication of the level of ovary tissue specific expression of the transcript compared to all the other tissue types tested in our assay. Thus, these experiments indicate Ovr107v1 being useful as an ovarian cancer diagnostic marker and/or therapeutic target.

Sensitivity and specificity data is reported in the table below.

	CLN	LNG	MAM	OVR	PRO
Sensitivity, Up vs. NAT	56%	44%	38%	0%	0%
Sensitivity, Down vs. NAT	11%	11%	25%	0%	0%
Sensitivity, Up vs. NRM	33%	44%	63%	77%	0%
Sensitivity, Down vs. NRM	44%	0%	25%	23%	0%
Specificity	25.86 %	21.26 %	22.86 %	25.15 %	21.59 %

Altogether, the tissue specificity, plus the mRNA differential expression in the samples tested are believed to make Ovr107v1 a good marker for diagnosing, monitoring, staging, imaging and/or treating ovarian cancer.

Primers used for QPCR Expression Analysis of Ovr107v1 are as follows:

(Ovr107v1_forward): CGCCTGACCCGACTGTCTTA (SEQ ID NO:329)

(Ovr107v1_reverse): GCTCAGATTCTGGCTCCAAGTCT (SEQ ID NO:330)

(Ovr107v1_probe): CCTACAGCAAAGCGCCCCCA (SEQ ID NO:331)

DEX0455_052.nt.4 (Ovr107v3)

The relative expression level of Ovr107v3 in various tissue samples is included below. Tissue samples include 73 pairs of matching samples, 11 non matched cancer samples, and 37 normal samples, all from various tissues annotated in the table. A matching pair is formed by mRNA from the cancer sample for a particular tissue and mRNA from the normal adjacent sample for that same tissue from the same individual. Of the normal samples 4 were blood samples which measured the expression levels in blood cells. Additionally, 2 prostatitis, and 4 Benign Prostatic Hyperplasia (BPH) samples are included. All the values are compared to ovarian cancer sample OVR8140 (calibrator).

The table below contains the relative expression level values for the sample as compared to the calibrator. The table includes the Sample ID, and expression level values for the following samples: Cancer (CAN), Normal Adjacent Tissue (NAT), Normal Tissue (NRM), Benign Prostatic Hyperplasia (BPH), and Prostatitis (PROST).

Sample	CAN	NAT	NRM	BPH	PROST
OVRA084	0.32	0.10			
OVRG010	0.01	4.12			
OVRG021	0.17	0.04			
OVR1157	2.88				
OVR7730	6.48				
OVR8140	1.00				
OVRC360	0.11				
OVR10050	1.56				
OVR10400	1.09				
OVR1050	0.68				
OVR130X	1.17				
OVR7180	0.79				
OVRA1B	1.43				
OVR247A			0.06		
OVR35GA			0.03		

OVRC087			0.03		
OVRC109			0.01		
OVR206I			0.08		
OVR5150			0.09		
OVR18GA			0.03		
OVR3370			0.00		
OVR1230			0.00		
OVRC177			0.04		
OVR40G			0.05		
BLD030B	0.16	0.00			
BLD520B	0.09	0.03			
BLDTR17	0.06	0.16			
CLN401C	0.09	0.10			
CLNAS43	0.24	0.03			
CLNAS98	0.14	0.11			
CLNCM12	0.05	0.11			
CLNDC19	0.40	0.14			
CLNRC01	0.05	0.07			
CLNRS53	0.06	0.16			
CLNSG27	0.11	0.12			
CLNTX01	0.07	0.02			
CVXKS52	0.50	1.56			
CVXNK23	0.51	2.02			
CVXNKS54	0.56	0.93			
CVXNKS55	1.32	3.28			
CVXNKS81	0.55	1.16			
ENDO10479	1.12	0.12			
ENDO28XA	1.33	0.11			
ENDO8XA	0.30	0.07			
KID106XD	0.01	0.03			
KID107XD	0.03	0.13			
KID109XD	0.25	0.04			
KID10XD	0.02	0.01			
KID22K	0.07	0.03			
LNG205L	0.03	0.05			
LNG315L	0.03	0.08			
LNG507L	0.58	0.07			
LNG528L	0.29	0.06			
LNG8837L	0.09	0.17			
LNGAC11	0.14	0.15			
LNGAC39	0.50	0.08			
LNGSQ80	0.18	0.22			
LNGSQ81	0.07	0.16			
LVR15XA	0.00	0.01			
LVR174L	0.01	0.01			
LVR187L	0.01	0.19			
MAM19DN	0.62	0.28			

MAM42DN	0.57	0.37			
MAM517	2.06	0.15			
MAM781M	0.07	0.06			
MAM869M	0.67	0.11			
MAM976M	0.60	0.16			
MAMS570	0.72	0.76			
MAMS699	0.10	0.46			
MAMS997	0.18	0.34			
PAN71XL	0.09	0.02			
PAN82XP	0.12				
PAN92X	2.58	0.00			
PRO23B	0.23	0.27			
PRO65XB	0.22	0.25			
PRO675P	0.40	0.19			
PRO84XB	0.34	0.42			
PRO958P	0.38	0.22			
PRO263C				0.30	
PRO276P				0.24	
PRO767B				0.93	
PRO855P				0.44	
PRO10R					0.32
PRO20R					0.19
SKN287S	0.86	0.00			
SKN39A	0.03	0.00			
SKN669S	0.12	0.40			
SMINT171S	0.21	0.04			
SMINT20SM	2.32	0.40			
SMINTH89	0.51	0.05			
STO261S	0.65	0.05			
STO288S	0.08	0.03			
STO88S	0.15	0.07			
THRD143N	0.09	0.73			
THRD270T	1.23	1.14			
THRD56T	0.64	0.18			
TST39X	0.07	0.02			
TST647T	0.11	0.01			
TST663T	0.12	0.03			
UTR135XO	0.13	0.27			
UTR85XU	0.15	0.09			
BLOB3			0.00		
BLOB6			0.69		
BLOB11			0.02		
BLO982B			0.10		
ADR48AD			0.02		
BRN10BR			0.01		
CLN01CL			0.05		
ESO01ES			0.93		

HRT46HR			0.00		
HUMREF00HR	0.09				
KID55KD			0.05		
LVR89LV			0.00		
LNG90LN			0.04		
MAM01MA			0.15		
MSL84MU			0.01		
OVR3APV			0.07		
PAN04PA			0.10		
PLA59PL			0.82		
PRO09PR			0.50		
REC21RC			0.26		
SMINT59SM			0.03		
SPL7GSP			0.03		
STO09ST			1.10		
THYM99TM			0.02		
TRA16TR			0.32		
TST4GTS			0.01		
UTR57UT			0.08		

Note: 0.00= Negative or Not Detected

The sensitivity for Ovr107v3 expression was calculated for the cancer samples versus normal samples. The sensitivity value indicates the percentage of cancer samples that show levels of Ovr107v3 at least 2 fold higher than the normal tissue or the corresponding normal adjacent form the same patient.

This specificity is an indication of the level of ovary tissue specific expression of the transcript compared to all the other tissue types tested in our assay. Thus, these experiments indicate Ovr107v3 being useful as an ovarian cancer diagnostic marker and/or therapeutic target.

Sensitivity and specificity data is reported in the table below.

	CLN	LNG	MAM	OVR	PRO
Sensitivity, Up vs. NAT	33%	33%	44%	0%	20%
Sensitivity, Down vs. NAT	22%	22%	11%	0%	0%
Sensitivity, Up vs. NRM	44%	67%	67%	92%	0%
Sensitivity, Down vs. NRM	0%	0%	11%	8%	40%
Specificity	8.79 %	10.44 %	33.52 %	43.35 %	21.74 %

Altogether, the tissue specificity, plus the mRNA differential expression in the samples tested are believed to make Ovr107v3 a good marker for diagnosing, monitoring, staging, imaging and/or treating ovarian cancer.

Primers used for QPCR Expression Analysis of Ovr107v3 are as follows:
(Ovr107v3_forward): CCTGCAGCCCAGAGCAAT (SEQ ID NO:332)
(Ovr107v3_reverse): GCTCAGATTCTGGCTCCAAGTC (SEQ ID NO:333)
(Ovr107v3_probe): ATCTCCAACCCTCCCGCTTCT (SEQ ID NO:334)

DEX0455_051.nt.6 (Ovr107v4)

The relative expression level of Ovr107v4 in various tissue samples is included below. Tissue samples include 69 pairs of matching samples, 15 non matched cancer samples, and 34 normal samples, all from various tissues annotated in the table. A matching pair is formed by mRNA from the cancer sample for a particular tissue and mRNA from the normal adjacent sample for that same tissue from the same individual. Of the normal samples 2 were blood samples which measured the expression levels in blood cells. Additionally, 2 prostatitis, and 4 Benign Prostatic Hyperplasia (BPH) samples are included. All the values are compared to breast normal sample MAM01MA (calibrator).

The table below contains the relative expression level values for the sample as compared to the calibrator. The table includes the Sample ID, and expression level values for the following samples: Cancer (CAN), Normal Adjacent Tissue (NAT), Normal Tissue (NRM), Benign Prostatic Hyperplasia (BPH), and Prostatitis (PROST).

Sample ID	CAN	NAT	NRM	BPH	PROST
OVRA084	1.03	0.60			
OVRG010	0.43	1.15			
OVRG021	0.72	1.63			
OVR1157	0.00				
OVR773O	2.63				
OVR814O	1.26				
OVRC360	0.46				
OVR1005O	13.92				
OVR1040O	6.00				
OVR105O	6.04				
OVR718O	4.15				
OVRA1B	3.67				
OVR247A			0.55		
OVR35GA			1.06		
OVRC087			0.35		
OVRC109			0.43		
OVR206I			0.93		
OVR515O			2.17		
OVR18GA			1.17		

OVRC177			0.68		
OVR40G			1.89		
OVRC004			0.00		
BLD030B	0.77	0.00			
BLD520B	2.75	0.88			
BLDTR17	0.70	2.67			
CLN401C	0.78	1.03			
CLNAS43	2.36	0.77			
CLNAS98	1.73	1.27			
CLNCM12	0.67	0.61			
CLNDC19	1.46	0.43			
CLNRC01	0.12	0.36			
CLNRS53	0.36	2.08			
CLNSG27	0.48	2.08			
CLNTX01	0.72	0.56			
CVXKS52	1.32	10.88			
CVXNK23	2.75				
CVXNKS54	1.33	10.06			
CVXNKS55	9.56	20.77			
CVXNKS81	3.27				
ENDO10479	3.77	4.17			
ENDO28XA	5.41	4.55			
ENDO8XA	1.21	1.31			
KID106XD	0.27	0.12			
KID107XD	0.60	0.45			
KID109XD	2.94	0.76			
KID10XD	0.18	0.28			
KID22K	0.80	0.15			
LNG205L	0.46	1.80			
LNG315L	0.37	2.06			
LNG507L	1.43				
LNG528L	1.26	0.85			
LNG8837L	0.86	1.74			
LNGAC11	0.77	1.37			
LNGAC39	1.28	1.22			
LNGSQ80	1.34	2.91			
LNGSQ81	0.95	1.01			
LVR15XA	0.05	0.06			
LVR174L	0.10	0.05			
LVR187L	0.00	0.86			
MAM19DN	1.31	3.79			
MAM42DN	1.98	3.48			
MAM517	3.35	0.00			
MAM781M	0.57	0.51			
MAM869M	2.29	1.06			
MAM976M	3.78	2.13			
MAMS570	2.14	3.13			

MAMS699	0.58	4.99			
MAMS997	2.72	1.84			
PAN71XL	0.76	0.24			
PAN82XP	1.49				
PAN92X	4.92				
PRO23B	0.87	1.01			
PRO65XB	0.62	0.72			
PRO675P	1.19	2.30			
PRO84XB	0.99	2.38			
PRO958P	1.31	1.39			
PRO263C				1.64	
PRO276P				0.60	
PRO767B				3.10	
PRO855P				0.92	
PRO10R					1.33
PRO20R					2.41
SKN287S	5.46	0.65			
SKN39A	2.56	0.22			
SKN669S	6.12	9.44			
SMINT171S	1.39	0.62			
SMINT20SM	7.46	2.59			
SMINTH89	0.97	0.16			
STO261S	4.97	3.16			
STO288S	0.23	0.40			
STO88S	3.10	0.38			
THRD143N	0.70	5.66			
THRD270T	11.59	12.76			
THRD56T	4.61	1.92			
TST39X	0.91	0.00			
TST647T	1.42	0.29			
TST663T	1.42	0.37			
UTR135XO	3.28	4.02			
UTR85XU	1.51	2.11			
BLOB3			0.25		
BLOB11			0.92		
ADR48AD			0.00		
BRN10BR			0.00		
CLN01CL			0.22		
ESO01ES			7.88		
HRT46HR			0.06		
HUMREF00HR	0.49				
KID55KD			0.10		
LVR89LV			0.03		
LNG90LN			0.26		
MAM01MA			1.00		
MSL84MU			0.06		
OVR3APV			1.02		

PAN04PA			0.14		
PLA59PL			2.01		
PRO09PR			0.57		
REC21RC			1.21		
SMINT59SM			0.11		
SPL7GSP			0.26		
STO09ST			1.56		
THYM99TM			0.20		
TRA16TR			1.45		
TST4GTS			0.19		
UTR57UT			1.28		

0.00= Negative or no expression

The sensitivity for Ovr107v4 expression was calculated for the cancer samples versus normal samples. The sensitivity value indicates the percentage of cancer samples that show levels of Ovr107v4 at least 2 fold higher than the normal tissue or the corresponding normal adjacent form the same patient.

This specificity is an indication of the level of ovary tissue specific expression of the transcript compared to all the other tissue types tested in our assay. Thus, these experiments indicate Ovr107v4 being useful as an ovarian cancer diagnostic marker and/or therapeutic target.

Sensitivity and specificity data is reported in the table below.

	CLN	LNG	MAM	OVR	PRO
Sensitivity, Up vs. NAT	22%	0%	22%	0%	0%
Sensitivity, Down vs. NAT	33%	50%	22%	0%	20%
Sensitivity, Up vs. NRM	78%	78%	56%	50%	40%
Sensitivity, Down vs. NRM	0%	0%	0%	25%	0%
Specificity	8.05%	8%	13.79%	13.17%	7.95%

Altogether, the tissue specificity, plus the mRNA differential expression in the samples tested are believed to make Ovr107v4 a good marker for diagnosing, monitoring, staging, imaging and/or treating ovarian cancer.

Primers used for QPCR Expression Analysis of Ovr107v4 are as follows:

(Ovr107v4_forward): GGAGCCCTGAGCATTGTAATATG (SEQ ID NO:335)

(Ovr107v4_reverse): CCCTGGTAGCCGGGTAGAG (SEQ ID NO:336)

(Ovr107v4_probe): CAGATGGTGTGCCAACTGCTGT (SEQ ID NO:337)

DEX0455_053.nt.2 (Ovr110v1)

The relative expression level of Ovr110v1 in various tissue samples is included below. Tissue samples include 74 pairs of matching samples, 11 non matched cancer samples, and 39 normal samples, all from various tissues annotated in the table. A matching pair is formed by mRNA from the cancer sample for a particular tissue and mRNA from the normal adjacent sample for that same tissue from the same individual. Of the normal samples 5 were blood samples which measured the expression levels in blood cells. Additionally, 2 prostatitis, and 4 Benign Prostatic Hyperplasia (BPH) samples are included. All the values are compared to breast normal sample MAM01MA (calibrator).

The table below contains the relative expression level values for the sample as compared to the calibrator. The table includes the Sample ID, and expression level values for the following samples: Cancer (CAN), Normal Adjacent Tissue (NAT), Normal Tissue (NRM), Benign Prostatic Hyperplasia (BPH), and Prostatitis (PROST).

Sample ID	CAN	NAT	NRM	BPH	PROST
OVRA084	0.00	0.00			
OVRG010	0.00	0.00			
OVRG021	0.00	0.00			
OVR1157	4.92				
OVR773O	4.23				
OVRC360	0.00				
OVR1005O	0.00				
OVR1040O	0.11				
OVR105O	0.00				
OVR130X	0.00				
OVR718O	0.33				
OVRA1B	0.07				
OVR35GA			0.00		
OVRC087			0.00		
OVRC109			0.00		
OVR206I			0.00		
OVR515O			0.00		
OVR18GA			0.00		
OVR337O			0.00		
OVR123O			0.00		
OVRC177			0.00		
OVR40G			0.00		
OVR451O			0.00		
BLD030B	0.00	0.53			
BLD520B	0.00	0.00			
BLDTR17	0.00	0.03			

CLN401C	0.00	0.00			
CLNAS43	0.00	0.00			
CLNAS98	0.00	0.00			
CLNCM12	0.00	0.00			
CLNDC19	0.00	0.00			
CLNRC01	0.00	0.00			
CLNRS53	0.00	0.00			
CLNSG27	0.00	0.00			
CLNTX01	0.00	0.00			
CVXKS52	0.00	0.00			
CVXNKS55	0.03	0.00			
CVXNKS25	0.00	0.29			
CVXNKS18	0.00	0.00			
CVXNKS54	0.00	0.00			
ENDO10479	0.10	0.00			
ENDO28XA	0.78	0.00			
ENDO8XA	0.00	0.01			
KID106XD	0.00	0.00			
KID12XD	0.01	0.15			
KID10XD	0.00	0.00			
KID22K	0.00	0.01			
KID107XD	0.00	0.01			
LNG205L	0.00	0.00			
LNG315L	0.00	0.00			
LNG507L	0.00	0.00			
LNG528L	0.00	0.00			
LNG8837L	0.21	0.00			
LNGAC11	0.01	0.00			
LNGAC39	0.00	0.00			
LNGSQ80	0.00	0.00			
LNGSQ81	0.08	0.00			
LVR15XA	0.00	0.00			
LVR174L	0.00	0.00			
LVR187L	0.00	0.03			
MAM19DN	0.36	1.23			
MAM42DN	0.09	0.00			
MAM517	0.00	0.00			
MAM781M	0.47	0.00			
MAM869M	0.46	0.00			
MAM976M	0.22	0.00			
MAMS570	0.55	0.45			
MAMS699	0.22	1.06			
MAMS997	0.73	0.21			
PAN71XL	0.00	0.00			
PAN77X	0.00				
PAN92X	0.00	0.00			
PRO10R					0.00

PRO20R					0.00
PRO23B	0.00	0.00			
PRO263C				0.00	
PRO276P				0.01	
PRO65XB	0.01	0.01			
PRO675P	0.00	0.00			
PRO767B				0.35	
PRO84XB	0.00	0.08			
PRO855P				0.00	
PRO958P	0.03	0.03			
SKN287S	0.00	0.00			
SKN39A	0.00	0.00			
SKN669S	0.00	0.00			
SMINT171S	0.00	0.00			
SMINT20SM	0.00	0.00			
SMINTH89	0.00	0.00			
STO261S	0.00	0.00			
STO288S	0.00	0.00			
STOAC93	0.00	0.00			
STO88S	0.00	0.00			
THRD143N	0.00	0.00			
THRD270T	0.00	0.00			
THRD56T	0.00	0.00			
TST39X	0.84	0.00			
TST647T	0.00	0.00			
TST663T	0.04	0.00			
UTR135XO	0.00	0.00			
UTR85XU	0.00	0.03			
BLOB3			0.00		
BLOB11			0.00		
BLO69			0.00		
BLO72			0.00		
BLO73			0.00		
ADR48AD			0.00		
BRN10BR			0.00		
CLN01CL			0.00		
CVX06CV			0.00		
ESO01ES			0.00		
HRT46HR			0.00		
HUMREF00HR	0.00				
KID55KD			0.00		
LVR89LV			0.00		
LNG90LN			0.00		
MAM01MA			1.00		
MSL84MU			0.00		
OVR3APV			0.00		
PAN04PA			0.00		

PLA59PL			0.00		
PRO09PR			0.51		
REC21RC			0.00		
SMINT59SM			0.00		
SPL7GSP			0.00		
STO09ST			0.00		
THYM99TM			0.00		
TRA16TR			0.15		
TST4GTS			0.15		
UTR57UT			0.00		

0.00= Negative or no expression

The sensitivity for Ovr110v1 expression was calculated for the cancer samples versus normal samples. The sensitivity value indicates the percentage of cancer samples that show levels of Ovr110v1 at least 2 fold higher than the normal tissue or the corresponding normal adjacent form the same patient.

This specificity is an indication of the level of ovary tissue specific expression of the transcript compared to all the other tissue types tested in our assay. Thus, these experiments indicate Ovr110v1 being useful as an ovarian cancer diagnostic marker and/or therapeutic target.

Sensitivity and specificity data is reported in the table below.

	CLN	LNG	MAM	OVR	PRO
Sensitivity, Up vs. NAT	0%	33%	56%	0%	0%
Sensitivity, Down vs. NAT	0%	0%	22%	0%	20%
Sensitivity, Up vs. NRM	0%	33%	0%	42%	0%
Sensitivity, Down vs. NRM	0%	0%	78%	0%	100%
Specificity	74.73 %	76.34 %	89.78 %	76.27 %	79.26 %

Altogether, the tissue specificity, plus the mRNA differential expression in the samples tested are believed to make Ovr110v1 a good marker for diagnosing, monitoring, staging, imaging and/or treating ovarian cancer.

Additionally, the tissue specificity, plus the mRNA differential expression in the samples tested may make Ovr110v1 a good marker for diagnosing, monitoring, staging, imaging and/or treating lung cancer.

Primers used for QPCR Expression Analysis of Ovr110v1 are as follows:

(Ovr110v1_forward): TCATTGGCTTTGGTATTTCAGAAG (SEQ ID NO:338)

(Ovr110v1_reverse): GTTCAGGAAGCAAAGATCAATGC (SEQ ID NO:339)

(Ovr110v1_probe): AGCAATGAAGGGTTTGGTTGTAGAAG (SEQ ID NO:340)

Conclusions

Altogether, the high level of tissue specificity, plus the mRNA overexpression in matched samples tested are indicative of SEQ ID NO: 1-128 being a diagnostic marker and/or a therapeutic target for cancer.

Example 3: Protein Expression

The OSNA is amplified by polymerase chain reaction (PCR) and the amplified DNA fragment encoding the OSNA is subcloned in pET-21d for expression in E. coli. In addition to the OSNA coding sequence, codons for two amino acids, Met-Ala, flanking the NH_2-terminus of the coding sequence of OSNA, and six histidines, flanking the COOH-terminus of the coding sequence of OSNA, are incorporated to serve as initiating Met/restriction site and purification tag, respectively.

An over-expressed protein band of the appropriate molecular weight may be observed on a Coomassie blue stained polyacrylamide gel. This protein band is confirmed by Western blot analysis using monoclonal antibody against 6X Histidine tag.

Large-scale purification of OSP is achieved using cell paste generated from 6-liter bacterial cultures, and purified using immobilized metal affinity chromatography (IMAC). Soluble fractions that are separated from total cell lysate were incubated with a nickel chelating resin. The column is packed and washed with five column volumes of wash buffer. OSP is eluted stepwise with various concentration imidazole buffers.

Example 4: Fusion Proteins

The human Fc portion of the IgG molecule can be PCR amplified, using primers that span the 5'and 3' ends of the sequence described below. These primers also should have convenient restriction enzyme sites that will facilitate cloning into an expression vector, preferably a mammalian expression vector. For example, if pC4 (Accession No. 209646) is used, the human Fc portion can be ligated into the BamHI cloning site. Note that the 3' BamHI site should be destroyed. Next, the vector containing the human Fc portion is re-restricted with BamHI, linearizing the vector, and a polynucleotide of the present invention, isolated by the PCR protocol described in Example 2, is ligated into this BamHI site. Note that the polynucleotide is cloned without a stop codon, otherwise a fusion protein will not be produced. If the naturally occurring signal sequence is used to

produce the secreted protein, pC4 does not need a second signal peptide. Alternatively, if the naturally occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. *See, e.g.*, WO 96/34891.

Example 5: Production of an Antibody from a Polypeptide

In general, such procedures involve immunizing an animal (preferably a mouse) with polypeptide or, more preferably, with a secreted polypeptide-expressing cell. Such cells may be cultured in any suitable tissue culture medium; however, it is preferable to culture cells in Earle's modified Eagle's medium supplemented with 10% fetal bovine serum (inactivated at about 56°C), and supplemented with about 10 g/1 of nonessential amino acids, about 1,000 U/ml of penicillin, and about 100, µg/ml of streptomycin. The splenocytes of such mice are extracted and fused with a suitable myeloma cell line. Any suitable myeloma cell line may be employed in accordance with the present invention; however, it is preferable to employ the parent myeloma cell line (SP20), available from the ATCC. After fusion, the resulting hybridoma cells are selectively maintained in HAT medium, and then cloned by limiting dilution as described by Wands *et al.*, *Gastroenterology* 80: 225-232 (1981).

The hybridoma cells obtained through such a selection are then assayed to identify clones which secrete antibodies capable of binding the polypeptide. Alternatively, additional antibodies capable of binding to the polypeptide can be produced in a two-step procedure using anti-idiotypic antibodies. Such a method makes use of the fact that antibodies are themselves antigens, and therefore, it is possible to obtain an antibody which binds to a second antibody. In accordance with this method, protein specific antibodies are used to immunize an animal, preferably a mouse. The splenocytes of such an animal are then used to produce hybridoma cells, and the hybridoma cells are screened to identify clones which produce an antibody whose ability to bind to the protein-specific antibody can be blocked by the polypeptide. Such antibodies comprise anti-idiotypic antibodies to the protein specific antibody and can be used to immunize an animal to induce formation of further protein-specific antibodies.

Example 6: Method of Determining Alterations in a Gene Corresponding to a Polynucleotide

RNA is isolated from individual patients or from a family of individuals that have a phenotype of interest. cDNA is then generated from these RNA samples using protocols

known in the art. *See*, Sambrook (2001), *supra*. The cDNA is then used as a template for PCR, employing primers surrounding regions of interest in SEQ ID NO: 1-128. Suggested PCR conditions consist of 35 cycles at 95°C for 30 seconds; 60-120 seconds at 52-58°C; and 60-120 seconds at 70°C, using buffer solutions described in Sidransky *et al.*, *Science* 252(5006): 706-9 (1991). *See also* Sidransky *et al.*, *Science* 278(5340): 1054-9 (1997).

PCR products are then sequenced using primers labeled at their 5' end with T4 polynucleotide kinase, employing SequiTherm Polymerase. (Epicentre Technologies). The intron-exon borders of selected exons are also determined and genomic PCR products analyzed to confirm the results. PCR products harboring suspected mutations are then cloned and sequenced to validate the results of the direct sequencing. PCR products is cloned into T-tailed vectors as described in Holton *et al., Nucleic Acids Res.*, 19: 1156 (1991) and sequenced with T7 polymerase (United States Biochemical). Affected individuals are identified by mutations not present in unaffected individuals.

Genomic rearrangements may also be determined. Genomic clones are nick-translated with digoxigenin deoxyuridine 5' triphosphate (Boehringer Manheim), and FISH is performed as described in Johnson *et al.*, *Methods Cell Biol.* 35: 73-99 (1991). Hybridization with the labeled probe is carried out using a vast excess of human cot-1 DNA for specific hybridization to the corresponding genomic locus.

Chromosomes are counterstained with 4,6-diamino-2-phenylidole and propidium iodide, producing a combination of C-and R-bands. Aligned images for precise mapping are obtained using a triple-band filter set (Chroma Technology, Brattleboro, VT) in combination with a cooled charge-coupled device camera (Photometrics, Tucson, AZ) and variable excitation wavelength filters. Johnson (1991). Image collection, analysis and chromosomal fractional length measurements are performed using the ISee Graphical Program System. (Inovision Corporation, Durham, NC.) Chromosome alterations of the genomic region hybridized by the probe are identified as insertions, deletions, and translocations. These alterations are used as a diagnostic marker for an associated disease.

Example 7: Method of Detecting Abnormal Levels of a Polypeptide in a Biological Sample

Antibody-sandwich ELISAs are used to detect polypeptides in a sample, preferably a biological sample. Wells of a microtiter plate are coated with specific antibodies, at a

final concentration of 0.2 to 10 ug/ml. The antibodies are either monoclonal or polyclonal and are produced by the method described above. The wells are blocked so that non-specific binding of the polypeptide to the well is reduced. The coated wells are then incubated for > 2 hours at RT with a sample containing the polypeptide. Preferably, serial dilutions of the sample should be used to validate results. The plates are then washed three times with deionized or distilled water to remove unbound polypeptide. Next, 50 µl of specific antibody-alkaline phosphatase conjugate, at a concentration of 25-400 ng, is added and incubated for 2 hours at room temperature. The plates are again washed three times with deionized or distilled water to remove unbound conjugate. 75 µl of 4-methylumbelliferyl phosphate (MUP) or p-nitrophenyl phosphate (NPP) substrate solution are added to each well and incubated 1 hour at room temperature.

The reaction is measured by a microtiter plate reader. A standard curve is prepared, using serial dilutions of a control sample, and polypeptide concentrations are plotted on the X-axis (log scale) and fluorescence or absorbance on the Y-axis (linear scale). The concentration of the polypeptide in the sample is calculated using the standard curve.

Example 8: Formulating a Polypeptide

The secreted polypeptide composition will be formulated and dosed in a fashion consistent with good medical practice, taking into account the clinical condition of the individual patient (especially the side effects of treatment with the secreted polypeptide alone), the site of delivery, the method of administration, the scheduling of administration, and other factors known to practitioners. The "effective amount" for purposes herein is thus determined by such considerations.

As a general proposition, the total pharmaceutically effective amount of secreted polypeptide administered parenterally per dose will be in the range of about 1, µg/kg/day to 10 mg/kg/day of patient body weight, although, as noted above, this will be subject to therapeutic discretion. More preferably, this dose is at least 0.01 mg/kg/day, and most preferably for humans between about 0.01 and 1 mg/kg/day for the hormone. If given continuously, the secreted polypeptide is typically administered at a dose rate of about 1 µg/kg/hour to about 50 mg/kg/hour, either by 1-4 injections per day or by continuous subcutaneous infusions, for example, using a mini-pump. An intravenous bag solution may also be employed. The length of treatment needed to observe changes and the

interval following treatment for responses to occur appears to vary depending on the desired effect.

Pharmaceutical compositions containing the secreted protein of the invention are administered orally, rectally, parenterally, intracistemally, intravaginally, intraperitoneally, topically (as by powders, ointments, gels, drops or transdermal patch), bucally, or as an oral or nasal spray. "Pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid or liquid filler, diluent, encapsulating material or formulation auxiliary of any type. The term "parenteral" as used herein refers to modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

The secreted polypeptide is also suitably administered by sustained-release systems. Suitable examples of sustained-release compositions include semipermeable polymer matrices in the form of shaped articles, e.g., films, or microcapsules. Sustained-release matrices include polylactides (U. S. Pat. No.3,773,919, EP 58,481, the contents of which are hereby incorporated by reference herein in their entirety), copolymers of L-glutamic acid and gamma-ethyl-L-glutamate (Sidman, U. et al., Biopolymers 22: 547-556 (1983)), poly (2-hydroxyethyl methacrylate) (R. Langer et al., J. Biomed. Mater. Res. 15: 167-277 (1981), and R. Langer, Chem. Tech. 12: 98-105 (1982)), ethylene vinyl acetate (R. Langer et al.) or poly-D- (-)-3-hydroxybutyric acid (EP 133,988). Sustained-release compositions also include liposomally entrapped polypeptides. Liposomes containing the secreted polypeptide are prepared by methods known per se: DE Epstein et al., Proc. Natl. Acad. Sci. USA 82: 3688-3692 (1985); Hwang et al., Proc. Natl. Acad. Sci. USA 77: 4030-4034 (1980); EP 52,322; EP 36,676; EP 88,046; EP 143,949; EP 142,641; Japanese Pat. Appl. 83-118008; U.S. Pat. Nos. 4,485,045 and 4,544,545; and EP 102,324, the contents of which are hereby incorporated by reference herein in their entirety. Ordinarily, the liposomes are of the small (about 200-800 Angstroms) unilamellar type in which the lipid content is greater than about 30 mol. percent cholesterol, the selected proportion being adjusted for the optimal secreted polypeptide therapy.

For parenteral administration, in one embodiment, the secreted polypeptide is formulated generally by mixing it at the desired degree of purity, in a unit dosage injectable form (solution, suspension, or emulsion), with a pharmaceutically acceptable carrier, i.e., one that is non-toxic to recipients at the dosages and concentrations employed and is compatible with other ingredients of the formulation.

For example, the formulation preferably does not include oxidizing agents and other compounds that are known to be deleterious to polypeptides. Generally, the formulations are prepared by contacting the polypeptide uniformly and intimately with liquid carriers or finely divided solid carriers or both. Then, if necessary, the product is shaped into the desired formulation. Preferably, the carrier is a parenteral carrier, more preferably, a solution that is isotonic with the blood of the recipient. Examples of such carrier vehicles include water, saline, Ringer's solution, and dextrose solution. Non-aqueous vehicles such as fixed oils and ethyl oleate are also useful herein, as well as liposomes.

The carrier suitably contains minor amounts of additives such as substances that enhance isotonicity and chemical stability. Such materials are non-toxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, succinate, acetic acid, and other organic acids or their salts; antioxidants such as ascorbic acid; low molecular weight (less than about ten residues) polypeptides, e. g., polyarginine or tripeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids, such as glycine, glutamic acid, aspartic acid, or arginine; monosaccharides, disaccharides, and other carbohydrates including cellulose or its derivatives, glucose, manose, or dextrins; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; counterions such as sodium; and/or nonionic surfactants such as polysorbates, poloxamers, or PEG.

The secreted polypeptide is typically formulated in such vehicles at a concentration of about 0.1 mg/ml to 100 mg/ml, preferably 1-10 mg/ml, at a pH of about 3 to 8. It will be understood that the use of certain of the foregoing excipients, carriers, or stabilizers will result in the formation of polypeptide salts.

Any polypeptide to be used for therapeutic administration can be sterile. Sterility is readily accomplished by filtration through sterile filtration membranes (e.g., 0.2 micron membranes). Therapeutic polypeptide compositions generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

Polypeptides ordinarily will be stored in unit or multi-dose containers, for example, sealed ampules or vials, as an aqueous solution or as a lyophilized formulation for reconstitution. As an example of a lyophilized formulation, 10-ml vials are filled with 5 ml of sterile-filtered 1 % (w/v) aqueous polypeptide solution, and the resulting mixture

is lyophilized. The infusion solution is prepared by reconstituting the lyophilized polypeptide using bacteriostatic Water-for-Injection.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Associated with such container (s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration. In addition, the polypeptides of the present invention may be employed in conjunction with other therapeutic compounds.

Example 9: Method of Treating Decreased Levels of the Polypeptide

It will be appreciated that conditions caused by a decrease in the standard or normal expression level of a secreted protein in an individual can be treated by administering the polypeptide of the present invention, preferably in the secreted form. Thus, the invention also provides a method of treatment of an individual in need of an increased level of the polypeptide comprising administering to such an individual a pharmaceutical composition comprising an amount of the polypeptide to increase the activity level of the polypeptide in such an individual.

For example, a patient with decreased levels of a polypeptide receives a daily dose 0.1-100 ug/kg of the polypeptide for six consecutive days. Preferably, the polypeptide is in the secreted form. The exact details of the dosing scheme, based on administration and formulation, are provided above.

Example 10: Method of Treating Increased Levels of the Polypeptide

Antisense or RNAi technology are used to inhibit production of a polypeptide of the present invention. This technology is one example of a method of decreasing levels of a polypeptide, preferably a secreted form, due to a variety of etiologies, such as cancer.

For example, a patient diagnosed with abnormally increased levels of a polypeptide is administered intravenously antisense polynucleotides at 0.5, 1.0, 1.5, 2.0 and 3.0 mg/kg day for 21 days. This treatment is repeated after a 7-day rest period if the treatment was well tolerated. The formulation of the antisense polynucleotide is provided above.

Example 11: Method of Treatment Using Gene Therapy

One method of gene therapy transplants fibroblasts, which are capable of expressing a polypeptide, onto a patient. Generally, fibroblasts are obtained from a subject by skin biopsy. The resulting tissue is placed in tissue-culture medium and separated into small pieces. Small chunks of the tissue are placed on a wet surface of a tissue culture flask, approximately ten pieces are placed in each flask. The flask is turned upside down, closed tight and left at room temperature over night. After 24 hours at room temperature, the flask is inverted and the chunks of tissue remain fixed to the bottom of the flask and fresh media (e. g., Ham's F12 media, with 10% FBS, penicillin and streptomycin) is added. The flasks are then incubated at 37°C for approximately one week.

At this time, fresh media is added and subsequently changed every several days. After an additional two weeks in culture, a monolayer of fibroblasts emerge. The monolayer is trypsinized and scaled into larger flasks. pMV-7 (Kirschmeier, P. T. et al., DNA, 7: 219-25 (1988)), flanked by the long terminal repeats of the Moloney murine sarcoma virus, is digested with EcoRI and HindIII and subsequently treated with calf intestinal phosphatase. The linear vector is fractionated on agarose gel and purified, using glass beads.

The cDNA encoding a polypeptide of the present invention can be amplified using PCR primers which correspond to the 5'and 3'end sequences respectively as set forth in Example 3. Preferably, the 5'primer contains an EcoRI site and the 3'primer includes a HindIII site. Equal quantities of the Moloney murine sarcoma virus linear backbone and the amplified EcoRI and HindIII fragment are added together, in the presence of T4 DNA ligase. The resulting mixture is maintained under conditions appropriate for ligation of the two fragments. The ligation mixture is then used to transform bacteria HB 101, which are then plated onto agar containing kanamycin for the purpose of confirming that the vector has the gene of interest properly inserted.

The amphotropic pA317 or GP+aml2 packaging cells are grown in tissue culture to confluent density in Dulbecco's Modified Eagles Medium (DMEM) with 10% calf serum (CS), penicillin and streptomycin. The MSV vector containing the gene is then added to the media and the packaging cells transduced with the vector. The packaging cells now produce infectious viral particles containing the gene (the packaging cells are now referred to as producer cells).

Fresh media is added to the transduced producer cells, and subsequently, the media is harvested from a 10 cm plate of confluent producer cells. The spent media, containing

the infectious viral particles, is filtered through a millipore filter to remove detached producer cells and this media is then used to infect fibroblast cells. Media is removed from a sub-confluent plate of fibroblasts and quickly replaced with the media from the producer cells. This media is removed and replaced with fresh media.

If the titer of virus is high, then virtually all fibroblasts will be infected and no selection is required. If the titer is very low, then it is necessary to use a retroviral vector that has a selectable marker, such as neo or his. Once the fibroblasts have been efficiently infected, the fibroblasts are analyzed to determine whether protein is produced.

The engineered fibroblasts are then transplanted onto the host, either alone or after having been grown to confluence on cytodex 3 microcarrier beads.

Example 12: Method of Treatment Using Gene Therapy-In Vivo

Another aspect of the present invention is using *in vivo* gene therapy methods to treat disorders, diseases and conditions. The gene therapy method relates to the introduction of naked nucleic acid (DNA, RNA, and antisense DNA or RNA) sequences into an animal to increase or decrease the expression of the polypeptide.

The polynucleotide of the present invention may be operatively linked to a promoter or any other genetic elements necessary for the expression of the polypeptide by the target tissue. Such gene therapy and delivery techniques and methods are known in the art, see, for example, Tabata H. *et al. Cardiovasc. Res.* 35 (3): 470-479 (1997); Chao J *et al.* Pharmacol. Res. 35 (6): 517-522 (1997); Wolff J. A. *Neuromuscul. Disord.* 7 (5): 314-318 (1997), Schwartz B. *et al. Gene Ther.* 3 (5): 405-411 (1996); and Tsurumi Y. *et al. Circulation* 94 (12): 3281-3290 (1996); W0 90/11092, W0 98/11779; U. S. Patent No. 5,693,622; 5,705,151; 5,580,859, the contents of which are hereby incorporated by reference herein in their entirety.

The polynucleotide constructs may be delivered by any method that delivers injectable materials to the cells of an animal, such as, injection into the interstitial space of tissues (heart, muscle, skin, ovarian, liver, intestine and the like). The polynucleotide constructs can be delivered in a pharmaceutically acceptable liquid or aqueous carrier.

The term "naked" polynucleotide, DNA or RNA, refers to sequences that are free from any delivery vehicle that acts to assist, promote, or facilitate entry into the cell, including viral sequences, viral particles, liposome formulations, lipofectin or precipitating agents and the like. However, the polynucleotides of the present invention may also be

delivered in liposome formulations (such as those taught in Felgner P. L. *et al. Ann. NY Acad. Sci.* 772: 126-139 (1995) and Abdallah B. *et al. Biol. Cell* 85 (1): 1-7 (1995)) which can be prepared by methods well known to those skilled in the art.

The polynucleotide vector constructs used in the gene therapy method are preferably constructs that will not integrate into the host genome nor will they contain sequences that allow for replication. Any strong promoter known to those skilled in the art can be used for driving the expression of DNA. Unlike other gene therapies techniques, one major advantage of introducing naked nucleic acid sequences into target cells is the transitory nature of the polynucleotide synthesis in the cells. Studies have shown that non-replicating DNA sequences can be introduced into cells to provide production of the desired polypeptide for periods of up to six months.

The polynucleotide construct can be delivered to the interstitial space of tissues within the an animal, including of muscle, skin, brain, ovarian, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus, rectum, nervous system, eye, gland, and connective tissue. Interstitial space of the tissues comprises the intercellular fluid, mucopolysaccharide matrix among the reticular fibers of organ tissues, elastic fibers in the walls of vessels or chambers, collagen fibers of fibrous tissues, or that same matrix within connective tissue ensheathing muscle cells or in the lacunae of bone. It is similarly the space occupied by the plasma of the circulation and the lymph fluid of the lymphatic channels. Delivery to the interstitial space of muscle tissue is preferred for the reasons discussed below. They may be conveniently delivered by injection into the tissues comprising these cells. They are preferably delivered to and expressed in persistent, non-dividing cells which are differentiated, although delivery and expression may be achieved in non-differentiated or less completely differentiated cells, such as, for example, stem cells of blood or skin fibroblasts. In vivo muscle cells are particularly competent in their ability to take up and express polynucleotides.

For the naked polynucleotide injection, an effective dosage amount of DNA or RNA will be in the range of from about 0.05 μg/kg body weight to about 50 mg/kg body weight. Preferably the dosage will be from about 0.005 mg/kg to about 20 mg/kg and more preferably from about 0.05 mg/kg to about 5 mg/kg. Of course, as the artisan of ordinary skill will appreciate, this dosage will vary according to the tissue site of injection. The appropriate and effective dosage of nucleic acid sequence can readily be determined

by those of ordinary skill in the art and may depend on the condition being treated and the route of administration. The preferred route of administration is by the parenteral route of injection into the interstitial space of tissues. However, other parenteral routes may also be used, such as, inhalation of an aerosol formulation particularly for delivery to ovarians or bronchial tissues, throat or mucous membranes of the nose. In addition, naked polynucleotide constructs can be delivered to arteries during angioplasty by the catheter used in the procedure.

The dose response effects of injected polynucleotide in muscle in vivo is determined as follows. Suitable template DNA for production of mRNA coding for polypeptide of the present invention is prepared in accordance with a standard recombinant DNA methodology. The template DNA, which may be either circular or linear, is either used as naked DNA or complexed with liposomes. The quadriceps muscles of mice are then injected with various amounts of the template DNA.

Five to six week old female and male Balb/C mice are anesthetized by intraperitoneal injection with 0.3 ml of 2.5% Avertin. A 1.5 cm incision is made on the anterior thigh, and the quadriceps muscle is directly visualized. The template DNA is injected in 0.1 ml of carrier in a 1 cc syringe through a 27 gauge needle over one minute, approximately 0.5 cm from the distal insertion site of the muscle into the knee and about 0.2 cm deep. A suture is placed over the injection site for future localization, and the skin is closed with stainless steel clips.

After an appropriate incubation time (e.g., 7 days) muscle extracts are prepared by excising the entire quadriceps. Every fifth 15 um cross-section of the individual quadriceps muscles is histochemically stained for protein expression. A time course for protein expression may be done in a similar fashion except that quadriceps from different mice are harvested at different times. Persistence of DNA in muscle following injection may be determined by Southern blot analysis after preparing total cellular DNA and HIRT supernatants from injected and control mice.

The results of the above experimentation in mice can be use to extrapolate proper dosages and other treatment parameters in humans and other animals using naked DNA.

Example 13: Transgenic Animals

The polypeptides of the invention can also be expressed in transgenic animals. Animals of any species, including, but not limited to, mice, rats, rabbits, hamsters, guinea

pigs, pigs, micro-pigs, goats, sheep, cows and non-human primates, e. g., baboons, monkeys, and chimpanzees may be used to generate transgenic animals. In a specific embodiment, techniques described herein or otherwise known in the art, are used to express polypeptides of the invention in humans, as part of a gene therapy protocol.

Any technique known in the art may be used to introduce the transgene (I. e., polynucleotides of the invention) into animals to produce the founder lines of transgenic animals. Such techniques include, but are not limited to, pronuclear microinjection (Paterson et al., *Appl. Microbiol. Biotechnol.* 40: 691-698 (1994); Carver et al., *Biotechnology* 11: 1263-1270 (1993); Wright et al., *Biotechnology* 9: 830-834 (1991); and U. S. Pat. No. 4,873,191, the contents of which is hereby incorporated by reference herein in its entirety); retrovirus mediated gene transfer into germ lines (Van der Putten et al., *Proc. Natl. Acad. Sci., USA* 82: 6148-6152 (1985)), blastocysts or embryos; gene targeting in embryonic stem cells (Thompson et al., *Cell* 56: 313-321 (1989)); electroporation of cells or embryos (Lo, 1983, *Mol Cell. Biol.* 3: 1803-1814 (1983)); introduction of the polynucleotides of the invention using a gene gun (see, e. g., Ulmer et al., *Science* 259: 1745 (1993); introducing nucleic acid constructs into embryonic pleuripotent stem cells and transferring the stem cells back into the blastocyst; and sperm mediated gene transfer (Lavitrano et al., *Cell* 57: 717-723 (1989). For a review of such techniques, see Gordon, "Transgenic Animals," *Intl. Rev. Cytol.* 115: 171-229 (1989).

Any technique known in the art may be used to produce transgenic clones containing polynucleotides of the invention, for example, nuclear transfer into enucleated oocytes of nuclei from cultured embryonic, fetal, or adult cells induced to quiescence (Campell *et al., Nature* 380: 64-66 (1996); Wilmut *et al., Nature* 385: 810813 (1997)).

The present invention provides for transgenic animals that carry the transgene in all their cells, as well as animals which carry the transgene in some, but not all their cells, I. e., mosaic animals or chimeric. The transgene may be integrated as a single transgene or as multiple copies such as in concatamers, e.g., head-to-head tandems or head-to-tail tandems. The transgene may also be selectively introduced into and activated in a particular cell type by following, for example, the teaching of Lasko et al. (Lasko et al., *Proc. Natl. Acad. Sci. USA* 89: 6232-6236 (1992)). The regulatory sequences required for such a cell-type specific activation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art. When it is desired that the polynucleotide transgene be integrated into the chromosomal site of the endogenous gene, gene targeting

is preferred. Briefly, when such a technique is to be utilized, vectors containing some nucleotide sequences homologous to the endogenous gene are designed for the purpose of integrating, via homologous recombination with chromosomal sequences, into and disrupting the function of the nucleotide sequence of the endogenous gene. The transgene may also be selectively introduced into a particular cell type, thus inactivating the endogenous gene in only that cell type, by following, for example, the teaching of Gu et al. (Gu et al., *Science* 265: 103-106 (1994)). The regulatory sequences required for such a cell-type specific inactivation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art.

Once transgenic animals have been generated, the expression of the recombinant gene may be assayed utilizing standard techniques. Initial screening may be accomplished by Southern blot analysis or PCR techniques to analyze animal tissues to verify that integration of the transgene has taken place. The level of mRNA expression of the transgene in the tissues of the transgenic animals may also be assessed using techniques which include, but are not limited to, Northern blot analysis of tissue samples obtained from the animal, in situ hybridization analysis, and reverse transcriptase-PCR (rt-PCR). Samples of transgenic gene-expressing tissue may also be evaluated immunocytochemically or immunohistochemically using antibodies specific for the transgene product.

Once the founder animals are produced, they may be bred, inbred, outbred, or crossbred to produce colonies of the particular animal. Examples of such breeding strategies include, but are not limited to: outbreeding of founder animals with more than one integration site in order to establish separate lines; inbreeding of separate lines in order to produce compound transgenics that express the transgene at higher levels because of the effects of additive expression of each transgene; crossing of heterozygous transgenic animals to produce animals homozygous for a given integration site in order to both augment expression and eliminate the need for screening of animals by DNA analysis; crossing of separate homozygous lines to produce compound heterozygous or homozygous lines; and breeding to place the transgene on a distinct background that is appropriate for an experimental model of interest.

Transgenic animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant

expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

Example 14: Knock-Out Animals

Endogenous gene expression can also be reduced by inactivating or "knocking out" the gene and/or its promoter using targeted homologous recombination. (E. g., see Smithies et al., Nature 317: 230-234 (1985); Thomas & Capecchi, Cell 51: 503512 (1987); Thompson et al., Cell 5: 313-321 (1989)) Alternatively, RNAi technology may be used. For example, a mutant, non-functional polynucleotide of the invention (or a completely unrelated DNA sequence) flanked by DNA homologous to the endogenous polynucleotide sequence (either the coding regions or regulatory regions of the gene) can be used, with or without a selectable marker and/or a negative selectable marker, to transfect cells that express polypeptides of the invention in vivo. In another embodiment, techniques known in the art are used to generate knockouts in cells that contain, but do not express the gene of interest. Insertion of the DNA construct, via targeted homologous recombination, results in inactivation of the targeted gene. Such approaches are particularly suited in research and agricultural fields where modifications to embryonic stem cells can be used to generate animal offspring with an inactive targeted gene (e. g., see Thomas & Capecchi 1987 and Thompson 1989, supra). However, this approach can be routinely adapted for use in humans provided the recombinant DNA constructs are directly administered or targeted to the required site in vivo using appropriate viral vectors that will be apparent to those of skill in the art.

In further embodiments of the invention, cells that are genetically engineered to express the polypeptides of the invention, or alternatively, that are genetically engineered not to express the polypeptides of the invention (e. g., knockouts) are administered to a patient in vivo. Such cells may be obtained from the patient (i.e., animal, including human) or an MHC compatible donor and can include, but are not limited to fibroblasts, bone marrow cells, blood cells (e. g., lymphocytes), adipocytes, muscle cells, endothelial cells etc. The cells are genetically engineered in vitro using recombinant DNA techniques to introduce the coding sequence of polypeptides of the invention into the cells, or alternatively, to disrupt the coding sequence and/or endogenous regulatory sequence associated with the polypeptides of the invention, e.g., by transduction (using viral vectors, and preferably vectors that integrate the transgene into the cell genome) or

transfection procedures, including, but not limited to, the use of plasmids, cosmids, YACs, naked DNA, electroporation, liposomes, etc.

The coding sequence of the polypeptides of the invention can be placed under the control of a strong constitutive or inducible promoter or promoter/enhancer to achieve expression, and preferably secretion, of the polypeptides of the invention. The engineered cells which express and preferably secrete the polypeptides of the invention can be introduced into the patient systemically, e. g., in the circulation, or intraperitoneally.

Alternatively, the cells can be incorporated into a matrix and implanted in the body, e. g., genetically engineered fibroblasts can be implanted as part of a skin graft; genetically engineered endothelial cells can be implanted as part of a lymphatic or vascular graft. (See, for example, Anderson et al. U. S. Patent No. 5,399,349; and Mulligan & Wilson, U. S. Patent No. 5,460,959, the contents of which are hereby incorporated by reference herein in their entirety).

When the cells to be administered are non-autologous or non-MHC compatible cells, they can be administered using well known techniques which prevent the development of a host immune response against the introduced cells. For example, the cells may be introduced in an encapsulated form which, while allowing for an exchange of components with the immediate extracellular environment, does not allow the introduced cells to be recognized by the host immune system.

Transgenic and "knock-out" animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

While preferred illustrative embodiments of the present invention are described, one skilled in the art will appreciate that the present invention can be practiced by other than the described embodiments, which are presented for purposes of illustration only and not by way of limitation. The present invention is limited only by the claims that follow.

We claim:

1. An isolated nucleic acid molecule comprising:

(a) a nucleic acid molecule comprising a nucleic acid sequence that encodes an amino acid sequence of SEQ ID NO: 129-295;

(b) a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-128;

(c) a nucleic acid molecule that selectively hybridizes to the nucleic acid molecule of (a) or (b); or

(d) a nucleic acid molecule having at least 95% sequence identity to the nucleic acid molecule of (a) or (b).

2. The nucleic acid molecule according to claim 1, wherein the nucleic acid molecule is a cDNA.

3. The nucleic acid molecule according to claim 1, wherein the nucleic acid molecule is genomic DNA.

4. The nucleic acid molecule according to claim 1, wherein the nucleic acid molecule is an RNA.

5. The nucleic acid molecule according to claim 1, wherein the nucleic acid molecule is a mammalian nucleic acid molecule.

6. The nucleic acid molecule according to claim 5, wherein the nucleic acid molecule is a human nucleic acid molecule.

7. A method for determining the presence of a ovarian specific nucleic acid (OSNA) in a sample, comprising the steps of:

(a) contacting the sample with the nucleic acid molecule of SEQ ID NO: 1-128 under conditions in which the nucleic acid molecule will selectively hybridize to an ovarian specific nucleic acid; and

(b) detecting hybridization of the nucleic acid molecule to an OSNA in the sample, wherein the detection of the hybridization indicates the presence of an OSNA in the sample.

8. A vector comprising the nucleic acid molecule of claim 1.

9. A host cell comprising the vector according to claim 8.

10. A method for producing a polypeptide encoded by the nucleic acid molecule according to claim 1, comprising the steps of:

(a) providing a host cell comprising the nucleic acid molecule operably linked to one or more expression control sequences, and

(b) incubating the host cell under conditions in which the polypeptide is produced.

11. A polypeptide encoded by the nucleic acid molecule according to claim 1.

12. An isolated polypeptide selected from the group consisting of:

(a) a polypeptide comprising an amino acid sequence with at least 95% sequence identity to of SEQ ID NO: 129-295 ; or

(b) a polypeptide comprising an amino acid sequence encoded by a nucleic acid molecule having at least 95% sequence identity to a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-128.

13. An antibody or fragment thereof that specifically binds to:

(a) a polypeptide comprising an amino acid sequence with at least 95% sequence identity to of SEQ ID NO: 129-295 ; or

(b) a polypeptide comprising an amino acid sequence encoded by a nucleic acid molecule having at least 95% sequence identity to a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-128.

14. A method for determining the presence of an ovarian specific protein in a sample, comprising the steps of:

(a) contacting the sample with a suitable reagent under conditions in which the reagent will selectively interact with the ovarian specific protein comprising an amino acid sequence with at least 95% sequence identity to of SEQ ID NO: 129-295; and

(b) detecting the interaction of the reagent with an ovarian specific protein in the sample, wherein the detection of binding indicates the presence of an ovarian specific protein in the sample.

15. A method for diagnosing or monitoring the presence and metastases of ovarian cancer in a patient, comprising the steps of:

(a) determining an amount of:

(i) a nucleic acid molecule comprising a nucleic acid sequence that encodes an amino acid sequence of SEQ ID NO: 129-295;

(ii) a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-128;

(iii) a nucleic acid molecule that selectively hybridizes to the nucleic acid molecule of (i) or (ii);

(iv) a nucleic acid molecule having at least 95% sequence identity to the nucleic acid molecule of (i) or (ii);

(v) a polypeptide comprising an amino acid sequence with at least 95% sequence identity to of SEQ ID NO: 129-295 ; or

(vi) a polypeptide comprising an amino acid sequence encoded by a nucleic acid molecule having at least 95% sequence identity to a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-128 and;

(b) comparing the amount of the determined nucleic acid molecule or the polypeptide in the sample of the patient to the amount of the ovarian specific marker in a normal control; wherein a difference in the amount of the nucleic acid molecule or the polypeptide in the sample compared to the amount of the nucleic acid molecule or the polypeptide in the normal control is associated with the presence of ovarian cancer.

16. A kit for detecting a risk of cancer or presence of cancer in a patient, said kit comprising a means for determining the presence of:

(a) a nucleic acid molecule comprising a nucleic acid sequence that encodes an amino acid sequence of SEQ ID NO: 129-295;

(b) a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-128;

(c) a nucleic acid molecule that selectively hybridizes to the nucleic acid molecule of (a) or (b); or

(d) a nucleic acid molecule having at least 95% sequence identity to the nucleic acid molecule of (a) or (b); or

(e) a polypeptide comprising an amino acid sequence with at least 95% sequence identity to of SEQ ID NO: 129-295 ; or

(f) a polypeptide comprising an amino acid sequence encoded by a nucleic acid molecule having at least 95% sequence identity to a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-128.

17. A method of treating a patient with ovarian cancer, comprising the step of administering a composition consisting of:

(a) a nucleic acid molecule comprising a nucleic acid sequence that encodes an amino acid sequence of SEQ ID NO: 129-295;

(b) a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-128;

(c) a nucleic acid molecule that selectively hybridizes to the nucleic acid molecule of (a) or (b);

(d) a nucleic acid molecule having at least 95% sequence identity to the nucleic acid molecule of (a) or (b);

(e) a polypeptide comprising an amino acid sequence with at least 95% sequence identity to of SEQ ID NO: 129-295 ; or

(f) a polypeptide comprising an amino acid sequence encoded by a nucleic acid molecule having at least 95% sequence identity to a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1-128;

to a patient in need thereof, wherein said administration induces an immune response against the ovarian cancer cell expressing the nucleic acid molecule or polypeptide.

18. A vaccine comprising the polypeptide or the nucleic acid encoding the polypeptide of claim 12.

FIGURE 1

```
EpCAM_nt       1                                                       0

Ovr232_nt      1 CAGATCTCAATTATCTAATTGCAATTGCAACGAGAACCAAAGCAGGGGAG    50

EpCAM_nt       1                                                       0

Ovr232_nt     51 CAGAGACAAACAATTTCTGAGGTAACCAGATGGCTTTATTAACTCAAGTT   100

EpCAM_nt       1                                                       0

Ovr232_nt    101 CTCACCTAAAATTGCCCTCAAGAATCCTGTGGGAATGGGTTGCAGTGGTG   150

EpCAM_nt       1                                                       0

Ovr232_nt    151 TGGCCCTGGATTCACAACCGACAGAGCTTCTGAATTCTGAGTGATCTGTA   200

EpCAM_nt       1                                                       0

Ovr232_nt    201 CACAAACACACCTCTGCCTGGGTTACACGCCTCCACGTTCCTCTATCCAG   250

EpCAM_nt       1                                                       0

Ovr232_nt    251 TTCCCGCACCCTTCCCCCCAGGCCCCATTCTTCAAGGCTTCAGAGCAGCG   300

EpCAM_nt       1                                                       0

Ovr232_nt    301 CTCCTCCGGTTAAAAGGAAGTCTCAGCACAGAATCTTCAAACCTCCTCGG   350

EpCAM_nt       1                                                       0

Ovr232_nt    351 AGGCCACCAAAGATCCCTAACGCCGCCATGGAGACGAAGCACCTGGGGCG   400

EpCAM_nt       1                                                       0

Ovr232_nt    401 GGGCGGAGCGGGGCGCGCGGGCCCACACCTGTGGAGAGGGCCGCGCCCCA   450

EpCAM_nt       1                                                       0

Ovr232_nt    451 ACTGCAGCGCCGGGGCTGGGGGAGGGGAGCCTACTCACTCCCCCAACTCC   500

EpCAM_nt       1                                                       0

Ovr232_nt    501 CGGGCGGTGACTCATCAACGAGCACCAGCGGCCAGAGGTGAGCAGTCCCG   550

EpCAM_nt       1                                                       0

Ovr232_nt    551 GGAAGGGGCCGAGAGGCGGGGCCGCCAGGTCGGGCAGGTGTGCGCTCCGC   600

EpCAM_nt       1                               CGGCGAGCGAGCACCTTCGAC    21
                                               |||||||||||||||||||||
Ovr232_nt    601 CCCGCCGCGCGCACAGAGCGCTAGTCCTTCGGCGAGCGAGCACCTTCGAC   650

EpCAM_nt      22 GCGGTCCGGGGACCCCCTCGTCGCTGTCCTCCCGACGCGGACCCGCGTGC    71
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt    651 GCGGTCCGGGGACCCCCTCGTCGCTGTCCTCCCGACGCGGACCCGCGTGC   700

EpCAM_nt      72 CCCAGGCCTCGCGCTGCCCGGCCGGCTCCTCGTGTCCCACTCCCGGCGCA   121
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt    701 CCCAGGCCTCGCGCTGCCCGGCCGGCTCCTCGTGTCCCACTCCCGGCGCA   750
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FIGURE 1 (continued)

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EpCAM_nt     122 CGCCCTCCCGCGAGTCCCGGGCCCCTCCCGCGCCCCTCTTCTCGGCGCGC   171
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt    751 CGCCCTCCCGCGAGTCCCGGGCCCCTCCCGCGCCCCTCTTCTCGGCGCGC   800

EpCAM_nt     172 GCGCAGCATGGCGCCCCCGCAGGTCCTCGCGTTCGGGCTTCTGCTTGCCG   221
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt    801 GCGCAGCATGGCGCCCCCGCAGGTCCTCGCGTTCGGGCTTCTGCTTGCCG   850

EpCAM_nt     222 CGGCGACGGCGACTTTTGCCGCAGCTCAGGAAGAATGTGTCTGTGAAAAC   271
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt    851 CGGCGACGGCGACTTTTGCCGCAGCTCAGGAAGAATGTGTCTGTGAAAAC   900

EpCAM_nt     272 TACAAGCTGGCCGTAAACTGCTTTGTGAATAATAATCGTCAATGCCAGTG   321
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt    901 TACAAGCTGGCCGTAAACTGCTTTGTGAATAATAATCGTCAATGCCAGTG   950

EpCAM_nt     322 TACTTCAGTTGGTGCACAAAATACTGTCATTTGCTCAAAGC---------   362
                 |||||||||||||||||||||||||||||||||||||||||
Ovr232_nt    951 TACTTCAGTTGGTGCACAAAATACTGTCATTTGCTCAAAGCGTGAGTAAA   1000

EpCAM_nt     363 --------------------------------------------------   362

Ovr232_nt   1001 ATATCCTAATTACCTGTAAGCTTTATTTTGACTTAATACTTCTTTAATTG   1050

EpCAM_nt     363 --------------------------------------------------   362

Ovr232_nt   1051 ATGTGCCTTGAGTTGGAAAGAGTTTTATTGGCTTAAATCTGAATCATGTT   1100

EpCAM_nt     363 --------------------------------------------------   362

Ovr232_nt   1101 ACAAAGTAAGTGTGGGAACACATAAATTTCAAATAATCTTTGACCCTGGA   1150

EpCAM_nt     363 --------------------------------------------------   362

Ovr232_nt   1151 ACTTTAGAGTTAATTTTTTTTTTCCCGTAATCATGAAATCAGTTATTTTT   1200

EpCAM_nt     363 ----------------------------TGGCTGCCAAATGTTTGGTGAT   384
                                             ||||||||||||||||||||||
Ovr232_nt   1201 CAGTTTGGCATTAAGGTTTCTTTTTCAGTGGCTGCCAAATGTTTGGTGAT   1250

EpCAM_nt     385 GAAGGCAGAAATGAATGGCTCAAAACTTGGGAGAAGAGCAAAACCTGAAG   434
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   1251 GAAGGCAGAAATGAATGGCTCAAAACTTGGGAGAAGAGCAAAACCTGAAG   1300

EpCAM_nt     435 GGGCCCTCCAGAACAATGATGGGCTTTATGATCCTGACTGCGATGAGAGC   484
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   1301 GGGCCCTCCAGAACAATGATGGGCTTTATGATCCTGACTGCGATGAGAGC   1350

EpCAM_nt     485 GGGCTCTTTAAGGCCAAGCAGTGCAACGGCACCTCCACGTGCTGGTGTGT   534
                 |||||||||||||||||||||||||||||||||||||.||||||||||||
Ovr232_nt   1351 GGGCTCTTTAAGGCCAAGCAGTGCAACGGCACCTCCATGTGCTGGTGTGT   1400

EpCAM_nt     535 GAACACTGCTGGGGTCAGAAGAACAGACAAGGACACTGAAATAACCTGCT   584
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   1401 GAACACTGCTGGGGTCAGAAGAACAGACAAGGACACTGAAATAACCTGCT   1450

EpCAM_nt     585 CTGAGCGAGTGAGAACCTACTGGATCATCATTGAACTAAAACACAAAGCA   634
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   1451 CTGAGCGAGTGAGAACCTACTGGATCATCATTGAACTAAAACACAAAGCA   1500
```

FIGURE 1 (continued)

```
EpCAM_nt     635 AGAGAAAAACCTTATGATAGTAAAAGTTTGCGGACTGCACTTCAGAAGGA  684
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   1501 AGAGAAAAACCTTATGATAGTAAAAGTTTGCGGACTGCACTTCAGAAGGA 1550

EpCAM_nt     685 GATCACAACGCGTTATCAACTGGATCCAAAATTTATCACGAGTATTTTGT  734
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   1551 GATCACAACGCGTTATCAACTGGATCCAAAATTTATCACGAGTATTTTGT 1600

EpCAM_nt     735 ATGAGAATAATGTTATCACTATTGATCTGGTTCAAAATTCTTCTCAAAAA  784
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   1601 ATGAGAATAATGTTATCACTATTGATCTGGTTCAAAATTCTTCTCAAAAA 1650

EpCAM_nt     785 ACTCAGAATGATGTGGACATAGCTGATGTGGCTTATTATTTTGAAAAAGA  834
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   1651 ACTCAGAATGATGTGGACATAGCTGATGTGGCTTATTATTTTGAAAAAGA 1700

EpCAM_nt     835 TGTTAAAGGTGAATCCTTGTTTCATTCTAAGAAAATGGACCTGACAGTAA  884
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   1701 TGTTAAAGGTGAATCCTTGTTTCATTCTAAGAAAATGGACCTGACAGTAA 1750

EpCAM_nt     885 ATGGGGAACAACTGGATCTGGATCCTGGTCAAACTTTAATTTATTATGTT  934
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   1751 ATGGGGAACAACTGGATCTGGATCCTGGTCAAACTTTAATTTATTATGTT 1800

EpCAM_nt     935 GATGAAAAAGCACCTGAATTCTCAATGCAGGGTCTAAAAGCTGGTGTTAT  984
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   1801 GATGAAAAAGCACCTGAATTCTCAATGCAGGGTCTAAAAGCTGGTGTTAT 1850

EpCAM_nt     985 TGCTGTTATTGTGGTTGTGGTGATAGCAGTTGTTGCTGGAATTGTTGTGC 1034
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   1851 TGCTGTTATTGTGGTTGTGGTGATAGCAGTTGTTGCTGGAATTGTTGTGC 1900

EpCAM_nt    1035 TGGTTATTTCCAGAAAGAAGAGAATGGCAAAGTATGAGAAGGCTGAGATA 1084
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   1901 TGGTTATTTCCAGAAAGAAGAGAATGGCAAAGTATGAGAAGGCTGAGATA 1950

EpCAM_nt    1085 AAGGAGATGGGTGAGATGCATAGGGAACTCAATGCATAACTATATAATTT 1134
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   1951 AAGGAGATGGGTGAGATGCATAGGGAACTCAATGCATAACTATATAATTT 2000

EpCAM_nt    1135 GAAGATTATAGAAGAAGGGAAATAGCAAATGGACACAAATTACAAATGTG 1184
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   2001 GAAGATTATAGAAGAAGGGAAATAGCAAATGGACACAAATTACAAATGTG 2050

EpCAM_nt    1185 TGTGCGTGGGACGAAGACATCTTTGAAGGTCATGAGTTTGTTAGTTTAAC 1234
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   2051 TGTGCGTGGGACGAAGACATCTTTGAAGGTCATGAGTTTGTTAGTTTAAC 2100

EpCAM_nt    1235 ATCATATATTTGTAATAGTGAAACCTGTACTCAAAATATAAGCAGCTTGA 1284
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   2101 ATCATATATTTGTAATAGTGAAACCTGTACTCAAAATATAAGCAGCTTGA 2150

EpCAM_nt    1285 AACTGGCTTTACCAATCTTGAAATTTGACCACAAGTGTCTTATATATGCA 1334
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   2151 AACTGGCTTTACCAATCTTGAAATTTGACCACAAGTGTCTTATATATGCA 2200

EpCAM_nt    1335 GATCTAATGTAAAATCCAGAACTTGGACTCCATCGTTAAAATTATTTATG 1384
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   2201 GATCTAATGTAAAATCCAGAACTTGGACTCCATCGTTAAAATTATTTATG 2250
```

FIGURE 1 (continued)

```
EpCAM_nt    1385 TGTAACATTCAAATGTGTGCATTAAATATGCTTCCACAGTAAAATCTGAA   1434
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   2251 TGTAACATTCAAATGTGTGCATTAAATATGCTTCCACAGTAAAATCTGAA   2300

EpCAM_nt    1435 AAACTGATTTGTGATTGAAAGCTGCCTTTCTATTTACTTGAGTCTTGTAC   1484
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   2301 AAACTGATTTGTGATTGAAAGCTGCCTTTCTATTTACTTGAGTCTTGTAC   2350

EpCAM_nt    1485 ATACATACTTTTTTATGAGCTATGAAATAAAACATTTTAAACTG         1528
                 ||||||||||||||||||||||||||||||||||||||||||||
Ovr232_nt   2351 ATACATACTTTTTTATGAGCTATGAAATAAAACATTTTAAACTGAA       2396
```

FIGURE 2

```
EpCAM_aa     1 MAPPQVLAFGLLLAAATATFAAAQEECVCENYKLAVNCFVNNNRQCQCTS   50
                                                             ..:.
Ovr232_aa    1                                               MKSV    4

EpCAM_aa    51 VGAQNTVICSKLAAKCLVMKAEMNGSKLGRRAKPEGALQNNDGLYDPDCD  100
               :......:...:||||||||||||||||||||||||||||||||||||||
Ovr232_aa    5 IFQFGIKVSFSVAAKCLVMKAEMNGSKLGRRAKPEGALQNNDGLYDPDCD   54

EpCAM_aa   101 ESGLFKAKQCNGTSTCWCVNTAGVRRTDKDTEITCSERVRTYWIIIELKH  150
               ||||||||||||||.|||||||||||||||||||||||||||||||||||
Ovr232_aa   55 ESGLFKAKQCNGTSMCWCVNTAGVRRTDKDTEITCSERVRTYWIIIELKH  104

EpCAM_aa   151 KAREKPYDSKSLRTALQKEITTRYQLDPKFITSILYENNVITIDLVQNSS  200
               ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_aa  105 KAREKPYDSKSLRTALQKEITTRYQLDPKFITSILYENNVITIDLVQNSS  154

EpCAM_aa   201 QKTQNDVDIADVAYYFEKDVKGESLFHSKKMDLTVNGEQLDLDPGQTLIY  250
               ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_aa  155 QKTQNDVDIADVAYYFEKDVKGESLFHSKKMDLTVNGEQLDLDPGQTLIY  204

EpCAM_aa   251 YVDEKAPEFSMQGLKAGVIAVIVVVVIAVVAGIVVLVISRKKRMAKYEKA  300
               ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232_aa  205 YVDEKAPEFSMQGLKAGVIAVIVVVVIAVVAGIVVLVISRKKRMAKYEKA  254

EpCAM_aa   301 EIKEMGEMHRELNA                                      314
               ||||||||||||||
Ovr232_aa  255 EIKEMGEMHRELNA                                      268
```

FIGURE 3

```
EpCAM_nt         1                                                     0

Ovr232V1_nt      1 CAGATCTCAATTATCTAATTGCAATTGCAACGAGAACCAAAGCAGGGGAG  50

EpCAM_nt         1                                                     0

Ovr232V1_nt     51 CAGAGACAAACAATTTCTGAGGTAACCAGATGGCTTTATTAACTCAAGTT  100

EpCAM_nt         1                                                     0

Ovr232V1_nt    101 CTCACCTAAAATTGCCCTCAAGAATCCTGTGGGAATGGGTTGCAGTGGTG  150

EpCAM_nt         1                                                     0

Ovr232V1_nt    151 TGGCCCTGGATTCACAACCGACAGAGCTTCTGAATTCTGAGTGATCTGTA  200

EpCAM_nt         1                                                     0

Ovr232V1_nt    201 CACAAACACACCTCTGCCTGGGTTACACGCCTCCACGTTCCTCTATCCAG  250

EpCAM_nt         1                                                     0

Ovr232V1_nt    251 TTCCCGCACCCTTCCCCCCAGGCCCCATTCTTCAAGGCTTCAGAGCAGCG  300

EpCAM_nt         1                                                     0

Ovr232V1_nt    301 CTCCTCCGGTTAAAAGGAAGTCTCAGCACAGAATCTTCAAACCTCCTCGG  350

EpCAM_nt         1                                                     0

Ovr232V1_nt    351 AGGCCACCAAAGATCCCTAACGCCGCCATGGAGACGAAGCACCTGGGGCG  400

EpCAM_nt         1                                                     0

Ovr232V1_nt    401 GGGCGGAGCGGGGCGCGCGGGCCCACACCTGTGGAGAGGGCCGCGCCCCA  450

EpCAM_nt         1                                                     0

Ovr232V1_nt    451 ACTGCAGCGCCGGGGCTGGGGGAGGGGAGCCTACTCACTCCCCCAACTCC  500

EpCAM_nt         1                             CGGCGAGCGAGCACCTTCGACG  22
                                               ||||.||
Ovr232V1_nt    501 CGGGCGGTGACTCATCAACGAGCACCAGCGGCCAG---------------  535

EpCAM_nt        23 CGGTCCGGGGACCCCCTCGTCGCTGTCCTCCCGACGCGGACCCGCGTGCC  72

Ovr232V1_nt    536 --------------------------------------------------  535

EpCAM_nt        73 CCAGGCCTCGCGCTGCCCGGCCGGCTCCTCGTGTCCCACTCCCGGCGCAC  122

Ovr232V1_nt    536 --------------------------------------------------  535

EpCAM_nt       123 GCCCTCCCGCGAGTCCCGGGCCCCTCCCGCGCCCCTCTTCTCGGCGCGCG  172

Ovr232V1_nt    536 --------------------------------------------------  535

EpCAM_nt       173 CGCAGCATGGCGCCCCCGCAGGTCCTCGCGTTCGGGCTTCTGCTTGCCGC  222

Ovr232V1_nt    536 --------------------------------------------------  535
```

FIGURE 3 (continued)

```
EpCAM_nt        223 GGCGACGGCGACTTTTGCCGCAGCTCAGGAAGAATGTGTCTGTGAAAACT  272
                                                 |||||||||||||||||||
Ovr232V1_nt     536 -------------------------------AGAATGTGTCTGTGAAAACT  555

EpCAM_nt        273 ACAAGCTGGCCGTAAACTGCTTTGTGAATAATAATCGTCAATGCCAGTGT  322
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt     556 ACAAGCTGGCCGTAAACTGCTTTGTGAATAATAATCGTCAATGCCAGTGT  605

EpCAM_nt        323 ACTTCAGTTGGTGCACAAAATACTGTCATTTGCTCAAAGCTGGCTGCCAA  372
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt     606 ACTTCAGTTGGTGCACAAAATACTGTCATTTGCTCAAAGCTGGCTGCCAA  655

EpCAM_nt        373 ATGTTTGGTGATGAAGGCAGAAATGAATGGCTCAAAACTTGGGAGAAGAG  422
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt     656 ATGTTTGGTGATGAAGGCAGAAATGAATGGCTCAAAACTTGGGAGAAGAG  705

EpCAM_nt        423 CAAAACCTGAAGGGGCCCTCCAGAACAATGATGGGCTTTATGATCCTGAC  472
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt     706 CAAAACCTGAAGGGGCCCTCCAGAACAATGATGGGCTTTATGATCCTGAC  755

EpCAM_nt        473 TGCGATGAGAGCGGGCTCTTTAAGGCCAAGCAGTGCAACGGCACCTCCAC  522
                    |||||||||||||||||||||||||||||||||||||||||||||||||.
Ovr232V1_nt     756 TGCGATGAGAGCGGGCTCTTTAAGGCCAAGCAGTGCAACGGCACCTCCAT  805

EpCAM_nt        523 GTGCTGGTGTGTGAACACTGCTGGGGTCAGAAGAACAGACAAGGACACTG  572
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt     806 GTGCTGGTGTGTGAACACTGCTGGGGTCAGAAGAACAGACAAGGACACTG  855

EpCAM_nt        573 AAATAACCTGCTCTGAGCGAGTGAGAACCTACTGGATCATCATTGAACTA  622
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt     856 AAATAACCTGCTCTGAGCGAGTGAGAACCTACTGGATCATCATTGAACTA  905

EpCAM_nt        623 AAACACAAAGCAAGAGAAAAACCTTATGATAGTAAAAGTTTGCGGACTGC  672
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt     906 AAACACAAAGCAAGAGAAAAACCTTATGATAGTAAAAGTTTGCGGACTGC  955

EpCAM_nt        673 ACTTCAGAAGGAGATCACAACGCGTTATCAACTGGATCCAAAATTTATCA  722
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt     956 ACTTCAGAAGGAGATCACAACGCGTTATCAACTGGATCCAAAATTTATCA 1005

EpCAM_nt        723 CGAGTATTTTGTATGAGAATAATGTTATCACTATTGATCTGGTTCAAAAT  772
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt    1006 CGAGTATTTTGTATGAGAATAATGTTATCACTATTGATCTGGTTCAAAAT 1055

EpCAM_nt        773 TCTTCTCAAAAAACTCAGAATGATGTGGACATAGCTGATGTGGCTTATTA  822
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt    1056 TCTTCTCAAAAAACTCAGAATGATGTGGACATAGCTGATGTGGCTTATTA 1105

EpCAM_nt        823 TTTTGAAAAAGATGTTAAAGGTGAATCCTTGTTTCATTCTAAGAAAATGG  872
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt    1106 TTTTGAAAAAGATGTTAAAGGTGAATCCTTGTTTCATTCTAAGAAAATGG 1155

EpCAM_nt        873 ACCTGACAGTAAATGGGGAACAACTGGATCTGGATCCTGGTCAAACTTTA  922
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt    1156 ACCTGACAGTAAATGGGGAACAACTGGATCTGGATCCTGGTCAAACTTTA 1205

EpCAM_nt        923 ATTTATTATGTTGATGAAAAAGCACCTGAATTCTCAATGCAGGGTCTAAA  972
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt    1206 ATTTATTATGTTGATGAAAAAGCACCTGAATTCTCAATGCAGGGTCTAAA 1255
```

FIGURE 3 (continued)

```
EpCAM_nt      973  AGCTGGTGTTATTGCTGTTATTGTGGTTGTGGTGATAGCAGTTGTTGCTG 1022
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt  1256  AGCTGGTGTTATTGCTGTTATTGTGGTTGTGGTGATAGCAGTTGTTGCTG 1305

EpCAM_nt     1023  GAATTGTTGTGCTGGTTATTTCCAGAAAGAAGAGAATGGCAAAGTATGAG 1072
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt  1306  GAATTGTTGTGCTGGTTATTTCCAGAAAGAAGAGAATGGCAAAGTATGAG 1355

EpCAM_nt     1073  AAGGCTGAGATAAAGGAGATGGGTGAGATGCATAGGGAACTCAATGCATA 1122
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt  1356  AAGGCTGAGATAAAGGAGATGGGTGAGATGCATAGGGAACTCAATGCATA 1405

EpCAM_nt     1123  ACTATATAATTTGAAGATTATAGAAGAAGGGAAATAGCAAATGGACACAA 1172
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt  1406  ACTATATAATTTGAAGATTATAGAAGAAGGGAAATAGCAAATGGACACAA 1455

EpCAM_nt     1173  ATTACAAATGTGTGTGCGTGGGACGAAGACATCTTTGAAGGTCATGAGTT 1222
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt  1456  ATTACAAATGTGTGTGCGTGGGACGAAGACATCTTTGAAGGTCATGAGTT 1505

EpCAM_nt     1223  TGTTAGTTTAACATCATATATTTGTAATAGTGAAACCTGTACTCAAAATA 1272
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt  1506  TGTTAGTTTAACATCATATATTTGTAATAGTGAAACCTGTACTCAAAATA 1555

EpCAM_nt     1273  TAAGCAGCTTGAAACTGGCTTTACCAATCTTGAAATTTGACCACAAGTGT 1322
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt  1556  TAAGCAGCTTGAAACTGGCTTTACCAATCTTGAAATTTGACCACAAGTGT 1605

EpCAM_nt     1323  CTTATATATGCAGATCTAATGTAAAATCCAGAACTTGGACTCCATCGTTA 1372
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt  1606  CTTATATATGCAGATCTAATGTAAAATCCAGAACTTGGACTCCATCGTTA 1655

EpCAM_nt     1373  AAATTATTTATGTGTAACATTCAAATGTGTGCATTAAATATGCTTCCACA 1422
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt  1656  AAATTATTTATGTGTAACATTCAAATGTGTGCATTAAATATGCTTCCACA 1705

EpCAM_nt     1423  GTAAAATCTGAAAAACTGATTTGTGATTGAAAGCTGCCTTTCTATTTACT 1472
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt  1706  GTAAAATCTGAAAAACTGATTTGTGATTGAAAGCTGCCTTTCTATTTACT 1755

EpCAM_nt     1473  TGAGTCTTGTACATACATACTTTTTTATGAGCTATGAAATAAAACATTTT 1522
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_nt  1756  TGAGTCTTGTACATACATACTTTTTTATGAGCTATGAAATAAAACATTTT 1805

EpCAM_nt     1523  AAACTG                                             1528
                   ||||||
Ovr232V1_nt  1806  AAACTGAA                                           1813
```

FIGURE 4

```
EpCAM_aa        1 MAPPQVLAFGLLLAAATATFAA                              22
                  .|............|.|...|.
Ovr232V1_aa     1 METKHLGRGGAGRAGPHLWRGPRPNCSAGAGGGEPTHSPNSRAVTHQRAP  50

EpCAM_aa       23 AQEECVCENYKLAVNCFVNNNRQCQCTSVGAQNTVICSKLAAKCLVMKAE  72
                  |..|||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_aa    51 AARECVCENYKLAVNCFVNNNRQCQCTSVGAQNTVICSKLAAKCLVMKAE 100

EpCAM_aa       73 MNGSKLGRRAKPEGALQNNDGLYDPDCDESGLFKAKQCNGTSTCWCVNTA 122
                  |||||||||||||||||||||||||||||||||||||||||||.||||||
Ovr232V1_aa   101 MNGSKLGRRAKPEGALQNNDGLYDPDCDESGLFKAKQCNGTSMCWCVNTA 150

EpCAM_aa      123 GVRRTDKDTEITCSERVRTYWIIIELKHKAREKPYDSKSLRTALQKEITT 172
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_aa   151 GVRRTDKDTEITCSERVRTYWIIIELKHKAREKPYDSKSLRTALQKEITT 200

EpCAM_aa      173 RYQLDPKFITSILYENNVITIDLVQNSSQKTQNDVDIADVAYYFEKDVKG 222
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_aa   201 RYQLDPKFITSILYENNVITIDLVQNSSQKTQNDVDIADVAYYFEKDVKG 250

EpCAM_aa      223 ESLFHSKKMDLTVNGEQLDLDPGQTLIYYVDEKAPEFSMQGLKAGVIAVI 272
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_aa   251 ESLFHSKKMDLTVNGEQLDLDPGQTLIYYVDEKAPEFSMQGLKAGVIAVI 300

EpCAM_aa      273 VVVVIAVVAGIVVLVISRKKRMAKYEKAEIKEMGEMHRELNA         314
                  ||||||||||||||||||||||||||||||||||||||||||
Ovr232V1_aa   301 VVVVIAVVAGIVVLVISRKKRMAKYEKAEIKEMGEMHRELNA         342
```

FIGURE 5

```
EpCAM_nt       1                                                      0
Ovr232V2_nt    1 CAGATCTCAATTATCTAATTGCAATTGCAACGAGAACCAAAGCAGGGGAG   0
EpCAM_nt       1                                                      0
Ovr232V2_nt   51 CAGAGACAAACAATTTCTGAGGTAACCAGATGGCTTTATTAACTCAAGTT  100
EpCAM_nt       1                                                      0
Ovr232V2_nt  101 CTCACCTAAAATTGCCCTCAAGAATCCTGTGGGAATGGGTTGCAGTGGTG  150
EpCAM_nt       1                                                      0
Ovr232V2_nt  151 TGGCCCTGGATTCACAACCGACAGAGCTTCTGAATTCTGAGTGATCTGTA  200
EpCAM_nt       1                                                      0
Ovr232V2_nt  201 CACAAACACACCTCTGCCTGGGTTACACGCCTCCACGTTCCTCTATCCAG  250
EpCAM_nt       1                                                      0
Ovr232V2_nt  251 TTCCCGCACCCTTCCCCCCAGGCCCCATTCTTCAAGGCTTCAGAGCAGCG  300
EpCAM_nt       1                                                      0
Ovr232V2_nt  301 CTCCTCCGGTTAAAAGGAAGTCTCAGCACAGAATCTTCAAACCTCCTCGG  350
EpCAM_nt       1                                                      0
Ovr232V2_nt  351 AGGCCACCAAAGATCCCTAACGCCGCCATGGAGACGAAGCACCTGGGGCG  400
EpCAM_nt       1                                                      0
Ovr232V2_nt  401 GGGCGGAGCGGGGCGCGCGGGCCCACACCTGTGGAGAGGGCCGCGCCCCA  450
EpCAM_nt       1                                                      0
Ovr232V2_nt  451 ACTGCAGCGCCGGGGCTGGGGGAGGGGAGCCTACTCACTCCCCCAACTCC  500
EpCAM_nt       1                                                      0
Ovr232V2_nt  501 CGGGCGGTGACTCATCAACGAGCACCAGCGGCCAGAGGTGAGCAGTCCCG  550
EpCAM_nt       1                                                      0
Ovr232V2_nt  551 GGAAGGGGCCGAGAGGCGGGGCCGCCAGGTCGGGCAGGTGTGCGCTCCGC  600
EpCAM_nt       1 CGGCGAGCGAGCACCTTCGAC                                21
                 |||||||||||||||||||||
Ovr232V2_nt  601 CCCGCCGCGCGCACAGAGCGCTAGTCCTTCGGCGAGCGAGCACCTTCGAC  650
EpCAM_nt      22 GCGGTCCGGGGACCCCCTCGTCGCTGTCCTCCCGACGCGGACCCGCGTGC   71
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V2_nt  651 GCGGTCCGGGGACCCCCTCGTCGCTGTCCTCCCGACGCGGACCCGCGTGC  700
EpCAM_nt      72 CCCAGGCCTCGCGCTGCCCGGCCGGCTCCTCGTGTCCCACTCCCGGCGCA   21
                 ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V2_nt  701 CCCAGGCCTCGCGCTGCCCGGCCGGCTCCTCGTGTCCCACTCCCGGCGCA  750
```

FIGURE 5 (continued)

```
EpCAM_nt       122  CGCCCTCCCGCGAGTCCCGGGCCCCTCCCGCGCCCCTCTTCTCGGCGCGC   171
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V2_nt    751  CGCCCTCCCGCGAGTCCCGGGCCCCTCCCGCGCCCCTCTTCTCGGCGCGC   800

EpCAM_nt       172  GCGCAGCATGGCGCCCCCGCAGGTCCTCGCGTTCGGGCTTCTGCTTGCCG   221
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V2_nt    801  GCGCAGCATGGCGCCCCCGCAGGTCCTCGCGTTCGGGCTTCTGCTTGCCG   850

EpCAM_nt       222  CGGCGACGGCGACTTTTGCCGCAGCTCAGGAAGAATGTGTCTGTGAAAAC   271
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V2_nt    851  CGGCGACGGCGACTTTTGCCGCAGCTCAGGAAGAATGTGTCTGTGAAAAC   900

EpCAM_nt       272  TACAAGCTGGCCGTAAACTGCTTTGTGAATAATAATCGTCAATGCCAGTG   321
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V2_nt    901  TACAAGCTGGCCGTAAACTGCTTTGTGAATAATAATCGTCAATGCCAGTG   950

EpCAM_nt       322  TACTTCAGTTGGTGCACAAAATACTGTCATTTGCTCAAAGCTGGCTGCCA   371
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V2_nt    951  TACTTCAGTTGGTGCACAAAATACTGTCATTTGCTCAAAGCTGGCTGCCA  1000

EpCAM_nt       372  AATGTTTGGTGATGAAGGCAGAAATGAATGGCTCAAAACTTGGGAGAAGA   421
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V2_nt   1001  AATGTTTGGTGATGAAGGCAGAAATGAATGGCTCAAAACTTGGGAGAAGA  1050

EpCAM_nt       422  GCAAAACCTGAAGGGGCCCTCCAGAACAATGATGGGCTTTATGATCCTGA   471
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V2_nt   1051  GCAAAACCTGAAGGGGCCCTCCAGAACAATGATGGGCTTTATGATCCTGA  1100

EpCAM_nt       472  CTGCGATGAGAGCGGGCTCTTTAAGGCCAAGCAGTGCAACGGCACCTCCA   521
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V2_nt   1101  CTGCGATGAGAGCGGGCTCTTTAAGGCCAAGCAGTGCAACGGCACCTCCA  1150

EpCAM_nt       522  CGTGCTGGTGTGTGAACACTGCTGGGGTCAGAAGAACAGACAAGGACACT   571
                    .|||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V2_nt   1151  TGTGCTGGTGTGTGAACACTGCTGGGGTCAGAAGAACAGACAAGGACACT  1200

EpCAM_nt       572  GAAATAACCTGCTCTGAGCGAGTGAGAACCTACTGGATCATCATTGAACT   621
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V2_nt   1201  GAAATAACCTGCTCTGAGCGAGTGAGAACCTACTGGATCATCATTGAACT  1250

EpCAM_nt       622  AAAACACAAAGCAAGAGAAAAACCTTATGATAGTAAAAGTTTGCGGACTG   671
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V2_nt   1251  AAAACACAAAGCAAGAGAAAAACCTTATGATAGTAAAAGTTTGCGGACTG  1300

EpCAM_nt       672  CACTTCAGAAGGAGATCACAACGCGTTATCAACTGGATCCAAAATTTATC   721
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V2_nt   1301  CACTTCAGAAGGAGATCACAACGCGTTATCAACTGGATCCAAAATTTATC  1350

EpCAM_nt       722  ACGAGTATTTTGTATGAGAATAATGTTATCACTATTGATCTGGTTCAAAA   771
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V2_nt   1351  ACGAGTATTTTGTATGAGAATAATGTTATCACTATTGATCTGGTTCAAAA  1400

EpCAM_nt       772  TTCTTCTCAAAAAACTCAGAATGATGTGGACATAGCTGATGTGGCTTATT   821
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V2_nt   1401  TTCTTCTCAAAAAACTCAGAATGATGTGGACATAGCTGATGTGGCTTATT  1450

EpCAM_nt       822  ATTTTGAAAAAGATGTTAAAGGTGAATCCTTGTTTCATTCTAAGAAAATG   871
                    |||||||||||||||.|....||......|||.|||..|.||..|...|.|
Ovr232V2_nt   1451  ATTTTGAAAAAGATGATGTGAGTATCATCTTCTTTATTCCTGTGTTCAGG  1500
```

FIGURE 5 (continued)

```
EpCAM_nt      872 GACCTGACAGTAAATGGGGAACAACTGGATCTGGATCCTGGTCAAACTTT  921
                  .|..|.........|||....|.......|..|..||............|||
Ovr232V2_nt  1501 AATGTAGTCTATCATGCCTCAATGAATTAAATATATTTCATCACCTTTTT 1550

EpCAM_nt      922 AATTTATTATGTTGATGAAAAAGCACCTGAATTCTCAATGCAGGGTCTAA  971
                  |.....|||...........|||......|......|..|..|...|.|..
Ovr232V2_nt  1551 ATCCACTTACAGATCAACCAAATGGTTCGCTGCTGCCGTTAATTTTGTCC 1600

EpCAM_nt      972 AAGCTGGTGTTATTGCTGTTATTGTGGTTGTGGTGATAGCAGTTGTTGCT 1021
                  ...|||....|.........|.|||....|.||...||....|....|..|
Ovr232V2_nt  1601 TCCCTGTCACTCACATGCATCTTGCTTGTTTGTATATTTATGCCTCTTAT 1650

EpCAM_nt     1022 GGAATTGTTGTGCTGGTTATTTCCAGAAAGAAGAGAATGGCAAAGTATGA 1071
                  ..|||||||.|||.....||.||..............||..........|.|
Ovr232V2_nt  1651 CAAATTGTTCTGCCTAAAATATCTCCCCTCTTTCTTATAATTCTTATTTA 1700

EpCAM_nt     1072 GAAGGCTGAGATAAAGGAGATGGGTGAGATGCATAGGGAACTCAATGCAT 1121
                  ..|..............|..|.|.|........|||.|...|.|.|||
Ovr232V2_nt  1701 TTATCTACTTGGTGGTTACTTAGTTTGTGCATATATGCTCCCCTATG--- 1747

EpCAM_nt     1122 AACTATATAATTTGAAGATTATAGAAGAAGGGAAATAGCAAATGGACACA 1171
                  |..|.|||||||||..|.|....|.|....|..|||.|..|.....||..|
Ovr232V2_nt  1748 ATATTTATAATTTACACAAATAAAAGTCTGTTAAAAAAGACTGTAACTGA 1797

EpCAM_nt     1172 AATTACAAATGTGTGTGCGTGGGACGAAGACATCTTTGAAGGTCATGAGT 1221
                  .||.|..||..|.|.|...||..||....|.||.||..|..|...|
Ovr232V2_nt  1798 TATGATTAAAATATTTTGTTGAAACTTTAATATATTATAGTGAGGT     1843

EpCAM_nt     1222 TTGTTAGTTTAACATCATATATTTGTAATAGTGAAACCTGTACTCAAAAT 1271

Ovr232V2_nt  1844                                                    1843

EpCAM_nt     1272 ATAAGCAGCTTGAAACTGGCTTTACCAATCTTGAAATTTGACCACAAGTG 1321

Ovr232V2_nt  1844                                                    1843

EpCAM_nt     1322 TCTTATATATGCAGATCTAATGTAAAATCCAGAACTTGGACTCCATCGTT 1371

Ovr232V2_nt  1844                                                    1843

EpCAM_nt     1372 AAAATTATTTATGTGTAACATTCAAATGTGTGCATTAAATATGCTTCCAC 1421

Ovr232V2_nt  1844
1843

EpCAM_nt     1422 AGTAAAATCTGAAAAACTGATTTGTGATTGAAAGCTGCCTTTCTATTTAC 1471

Ovr232V2_nt  1844                                                    1843

EpCAM_nt     1472 TTGAGTCTTGTACATACATACTTTTTATGAGCTATGAAATAAAACATTT 1521

Ovr232V2_nt  1844                                                    1843

EpCAM_nt     1522 TAAACTG                                            1528

Ovr232V2_nt  1844                                                    1843
```

FIGURE 6

```
EpCAM_aa        1  MAPPQVLAFGLLLAAATATFAAAQEECVCENYKLAVNCFVNNNRQCQCTS   50
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V2_aa     1  MAPPQVLAFGLLLAAATATFAAAQEECVCENYKLAVNCFVNNNRQCQCTS   50

EpCAM_aa       51  VGAQNTVICSKLAAKCLVMKAEMNGSKLGRRAKPEGALQNNDGLYDPDCD  100
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V2_aa    51  VGAQNTVICSKLAAKCLVMKAEMNGSKLGRRAKPEGALQNNDGLYDPDCD  100

EpCAM_aa      101  ESGLFKAKQCNGTSTCWCVNTAGVRRTDKDTEITCSERVRTYWIIIELKH  150
                   ||||||||||||||.|||||||||||||||||||||||||||||||||||
Ovr232V2_aa   101  ESGLFKAKQCNGTSMCWCVNTAGVRRTDKDTEITCSERVRTYWIIIELKH  150

EpCAM_aa      151  KAREKPYDSKSLRTALQKEITTRYQLDPKFITSILYENNVITIDLVQNSS  200
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V2_aa   151  KAREKPYDSKSLRTALQKEITTRYQLDPKFITSILYENNVITIDLVQNSS  200

EpCAM_aa      201  QKTQNDVDIADVAYYFEKDVKGESLFHSKKMDLTVNGEQLDLDPGQTLIY  250
                   ||||||||||||||||||......|.....::..:....
Ovr232V2_aa   201  QKTQNDVDIADVAYYFEKDDVSIIFFIPVFRNVVYHASMN            240

EpCAM_aa      251  YVDEKAPEFSMQGLKAGVIAVIVVVVIAVVAGIVVLVISRKKRMAKYEKA  300

Ovr232V2_aa   241                                                      240

EpCAM_aa      301  EIKEMGEMHRELNA                                      314

Ovr232V2_aa   241                                                      240
```

FIGURE 7

```
EpCAM_nt      1                                                     0

Ovr232V3_nt   1 CAGATCTCAATTATCTAATTGCAATTGCAACGAGAACCAAAGCAGGGGAG   50

EpCAM_nt      1                                                     0

Ovr232V3_nt  51 CAGAGACAAACAATTTCTGAGGTAACCAGATGGCTTTATTAACTCAAGTT  100

EpCAM_nt      1                                                     0

Ovr232V3_nt 101 CTCACCTAAAATTGCCCTCAAGAATCCTGTGGGAATGGGTTGCAGTGGTG  150

EpCAM_nt      1

Ovr232V3_nt 151 TGGCCCTGGATTCACAACCGACAGAGCTTCTGAATTCTGAGTGATCTGTA  200

EpCAM_nt      1                                                     0

Ovr232V3_nt 201 CACAAACACACCTCTGCCTGGGTTACACGCCTCCACGTTCCTCTATCCAG   50

EpCAM_nt      1                                                     0

Ovr232V3_nt 251 TTCCCGCACCCTTCCCCCAGGCCCCATTCTTCAAGGCTTCAGAGCAGCG  300

EpCAM_nt      1                                                     0

Ovr232V3_nt 301 CTCCTCCGGTTAAAAGGAAGTCTCAGCACAGAATCTTCAAACCTCCTCGG  350

EpCAM_nt      1                                                     0

Ovr232V3_nt 351 AGGCCACCAAAGATCCCTAACGCCGCCATGGAGACGAAGCACCTGGGGCG  400

EpCAM_nt      1                                                     0

Ovr232V3_nt 401 GGGCGGAGCGGGGCGCGCGGGCCCACACCTGTGGAGAGGGCCGCGCCCCA  450

EpCAM_nt      1                                                     0

Ovr232V3_nt 451 ACTGCAGCGCCGGGGCTGGGGGAGGGGAGCCTACTCACTCCCCCAACTCC  500

EpCAM_nt      1                                                     0

Ovr232V3_nt 501 CGGGCGGTGACTCATCAACGAGCACCAGCGGCCAGAGGTGAGCAGTCCCG  550

EpCAM_nt      1                                                     0

Ovr232V3_nt 551 GGAAGGGGCCGAGAGGCGGGGCCGCCAGGTCGGGCAGGTGTGCGCTCCGC  600

EpCAM_nt      1 CGGCGAGCGAGCACCTTCGAC                                21
                |||||||||||||||||||||
Ovr232V3_nt 601 CCCGCCGCGCGCACAGAGCGCTAGTCCTTCGGCGAGCGAGCACCTTCGAC  650

EpCAM_nt     22 GCGGTCCGGGGACCCCCTCGTCGCTGTCCTCCCGACGCGGACCCGCGTGC   71
                ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt 651 GCGGTCCGGGGACCCCCTCGTCGCTGTCCTCCCGACGCGGACCCGCGTGC  700

EpCAM_nt     72 CCCAGGCCTCGCGCTGCCCGGCCGGCTCCTCGTGTCCCACTCCCGGCGCA  121
                ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt 701 CCCAGGCCTCGCGCTGCCCGGCCGGCTCCTCGTGTCCCACTCCCGGCGCA  750
```

FIGURE 7 (continued)

```
EpCAM_nt      122  CGCCCTCCCGCGAGTCCCGGGCCCCTCCCGCGCCCCTCTTCTCGGCGCGC  171
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt   751  CGCCCTCCCGCGAGTCCCGGGCCCCTCCCGCGCCCCTCTTCTCGGCGCGC  800

EpCAM_nt      172  GCGCAGCATGGCGCCCCCGCAGGTCCTCGCGTTCGGGCTTCTGCTTGCCG  221
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt   801  GCGCAGCATGGCGCCCCCGCAGGTCCTCGCGTTCGGGCTTCTGCTTGCCG  850

EpCAM_nt      222  CGGCGACGGCGACTTTTGCCGCAGCTCAGGAA------------------  253
                   ||||||||||||||||||||||||||||||||
Ovr232V3_nt   851  CGGCGACGGCGACTTTTGCCGCAGCTCAGGAAGGTGAGGCGCGGATTGGA  900

EpCAM_nt      254  --------------------------------------------------  253

Ovr232V3_nt   901  GCAGAGTTGTGGAGCTGGGCTGGGCTGGGGGGCAGCGGCCCCCGGCCCTC  950

EpCAM_nt      254  --------------------------------------------------  253

Ovr232V3_nt   951  GGCCCCCGAAACGGGCATAATAGGGAGGGGACCAAGAGGCCGCGCTTTCC 1000

EpCAM_nt      254  --------------------------------------------------  253

Ovr232V3_nt  1001  AGCGTGGAGACCGGACGGTGCGGCCGTGCTCCGGCTCAGGCCCTCCGCGC 1050

EpCAM_nt      254  --------------------------------------------------  253

Ovr232V3_nt  1051  GGTAGGAAACGGCGAGGGCCGTCCCGGGGAGCAGCCTCACTTCGCAGCTT 1100

EpCAM_nt      254  ----------GAATGTGTCTGTGAAAACTACAAGCTGGCCGTAAACTGCT  293
                   ||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt  1101  TGCTCGCCTTGAATGTGTCTGTGAAAACTACAAGCTGGCCGTAAACTGCT 1150

EpCAM_nt      294  TTGTGAATAATAATCGTCAATGCCAGTGTACTTCAGTTGGTGCACAAAAT  343
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt  1151  TTGTGAATAATAATCGTCAATGCCAGTGTACTTCAGTTGGTGCACAAAAT 1200

EpCAM_nt      344  ACTGTCATTTGCTCAAAGCTGGCTGCCAAATGTTTGGTGATGAAGGCAGA  393
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt  1201  ACTGTCATTTGCTCAAAGCTGGCTGCCAAATGTTTGGTGATGAAGGCAGA 1250

EpCAM_nt      394  AATGAATGGCTCAAAACTTGGGAGAAGAGCAAAACCTGAAGGGGCCCTCC  443
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt  1251  AATGAATGGCTCAAAACTTGGGAGAAGAGCAAAACCTGAAGGGGCCCTCC 1300

EpCAM_nt      444  AGAACAATGATGGGCTTTATGATCCTGACTGCGATGAGAGCGGGCTCTTT  493
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt  1301  AGAACAATGATGGGCTTTATGATCCTGACTGCGATGAGAGCGGGCTCTTT 1350

EpCAM_nt      494  AAGGCCAAGCAGTGCAACGGCACCTCCACGTGCTGGTGTGTGAACACTGC  543
                   |||||||||||||||||||||||||||||.||||||||||||||||||||
Ovr232V3_nt  1351  AAGGCCAAGCAGTGCAACGGCACCTCCATGTGCTGGTGTGTGAACACTGC 1400

EpCAM_nt      544  TGGGGTCAGAAGAACAGACAAGGACACTGAAATAACCTGCTCTGAGCGAG  593
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt  1401  TGGGGTCAGAAGAACAGACAAGGACACTGAAATAACCTGCTCTGAGCGAG 1450

EpCAM_nt      594  TGAGAACCTACTGGATCATCATTGAACTAAAACACAAAGCAAGAGAAAAA  643
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt  1451  TGAGAACCTACTGGATCATCATTGAACTAAAACACAAAGCAAGAGAAAAA 1500
```

FIGURE 7 (continued)

```
EpCAM_nt       644  CCTTATGATAGTAAAAGTTTGCGGACTGCACTTCAGAAGGAGATCACAAC   693
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt   1501  CCTTATGATAGTAAAAGTTTGCGGACTGCACTTCAGAAGGAGATCACAAC  1550

EpCAM_nt       694  GCGTTATCAACTGGATCCAAAATTTATCACGAGTATTTTGTATGAGAATA   743
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt   1551  GCGTTATCAACTGGATCCAAAATTTATCACGAGTATTTTGTATGAGAATA  1600

EpCAM_nt       744  ATGTTATCACTATTGATCTGGTTCAAAATTCTTCTCAAAAAACTCAGAAT   793
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt   1601  ATGTTATCACTATTGATCTGGTTCAAAATTCTTCTCAAAAAACTCAGAAT  1650

EpCAM_nt       794  GATGTGGACATAGCTGATGTGGCTTATTATTTTGAAAAAGATGTTAAAGG   843
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt   1651  GATGTGGACATAGCTGATGTGGCTTATTATTTTGAAAAAGATGTTAAAGG  1700

EpCAM_nt       844  TGAATCCTTGTTTCATTCTAAGAAAATGGACCTGACAGTAAATGGGGAAC   893
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt   1701  TGAATCCTTGTTTCATTCTAAGAAAATGGACCTGACAGTAAATGGGGAAC  1750

EpCAM_nt       894  AACTGGATCTGGATCCTGGTCAAACTTTAATTTATTATGTTGATGAAAAA   943
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt   1751  AACTGGATCTGGATCCTGGTCAAACTTTAATTTATTATGTTGATGAAAAA  1800

EpCAM_nt       944  GCACCTGAATTCTCAATGCAGGGTCTAAAAGCTGGTGTTATTGCTGTTAT   993
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt   1801  GCACCTGAATTCTCAATGCAGGGTCTAAAAGCTGGTGTTATTGCTGTTAT  1850

EpCAM_nt       994  TGTGGTTGTGGTGATAGCAGTTGTTGCTGGAATTGTTGTGCTGGTTATTT  1043
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt   1851  TGTGGTTGTGGTGATAGCAGTTGTTGCTGGAATTGTTGTGCTGGTTATTT  1900

EpCAM_nt      1044  CCAGAAAGAAGAGAATGGCAAAGTATGAGAAGGCTGAGATAAAGGAGATG  1093
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt   1901  CCAGAAAGAAGAGAATGGCAAAGTATGAGAAGGCTGAGATAAAGGAGATG  1950

EpCAM_nt      1094  GGTGAGATGCATAGGGAACTCAATGCATAACTATATAATTTGAAGATTAT  1143
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt   1951  GGTGAGATGCATAGGGAACTCAATGCATAACTATATAATTTGAAGATTAT  2000

EpCAM_nt      1144  AGAAGAAGGGAAATAGCAAATGGACACAAATTACAAATGTGTGTGCGTGG  1193
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt   2001  AGAAGAAGGGAAATAGCAAATGGACACAAATTACAAATGTGTGTGCGTGG  2050

EpCAM_nt      1194  GACGAAGACATCTTTGAAGGTCATGAGTTTGTTAGTTTAACATCATATAT  1243
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt   2051  GACGAAGACATCTTTGAAGGTCATGAGTTTGTTAGTTTAACATCATATAT  2100

EpCAM_nt      1244  TTGTAATAGTGAAACCTGTACTCAAAATATAAGCAGCTTGAAACTGGCTT  1293
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt   2101  TTGTAATAGTGAAACCTGTACTCAAAATATAAGCAGCTTGAAACTGGCTT  2150

EpCAM_nt      1294  TACCAATCTTGAAATTTGACCACAAGTGTCTTATATATGCAGATCTAATG  1343
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt   2151  TACCAATCTTGAAATTTGACCACAAGTGTCTTATATATGCAGATCTAATG  2200

EpCAM_nt      1344  TAAAATCCAGAACTTGGACTCCATCGTTAAAATTATTTATGTGTAACATT  1393
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt   2201  TAAAATCCAGAACTTGGACTCCATCGTTAAAATTATTTATGTGTAACATT  2250
```

FIGURE 7 (continued)

```
EpCAM_nt     1394 CAAATGTGTGCATTAAATATGCTTCCACAGTAAAATCTGAAAAACTGATT 1443
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt  2251 CAAATGTGTGCATTAAATATGCTTCCACAGTAAAATCTGAAAAACTGATT 2300

EpCAM_nt     1444 TGTGATTGAAAGCTGCCTTTCTATTTACTTGAGTCTTGTACATACATACT 1493
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_nt  2301 TGTGATTGAAAGCTGCCTTTCTATTTACTTGAGTCTTGTACATACATACT 2350

EpCAM_nt     1494 TTTTTATGAGCTATGAAATAAAACATTTTAAACTG                1528
                  |||||||||||||||||||||||||||||||||||
Ovr232V3_nt  2351 TTTTTATGAGCTATGAAATAAAACATTTTAAACTGAA              2387
```

FIGURE 8

```
EpCAM_aa         1 MAPPQVLAFGLLLAAATATFAAAQE-------------------------  25
                   |||||||||||||||||||||||||
Ovr232V3_aa      1 MAPPQVLAFGLLLAAATATFAAAQEGEARIGAKLWSWAGLGGNGPRPSAP  50

EpCAM_aa        26 --------------------------------------------------  25

Ovr232V3_aa     51 ETGIIGRGPRGRAFQRGDRTVRPCSGSGPPRGRKRRGPSRGAASLRSFAR 100

EpCAM_aa        26 -ECVCENYKLAVNCFVNNNRQCQCTSVGAQNTVICSKLAAKCLVMKAEMN  74
                    |||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_aa    101 LECVCENYKLAVNCFVNNNRQCQCTSVGAQNTVICSKLAAKCLVMKAEMN 150

EpCAM_aa        75 GSKLGRRAKPEGALQNNDGLYDPDCDESGLFKAKQCNGTSTCWCVNTAGV 124
                   ||||||||||||||||||||||||||||||||||||||||.|||||||||
Ovr232V3_aa    151 GSKLGRRAKPEGALQNNDGLYDPDCDESGLFKAKQCNGTSMCWCVNTAGV 200

EpCAM_aa       125 RRTDKDTEITCSERVRTYWIIIELKHKAREKPYDSKSLRTALQKEITTRY 174
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_aa    201 RRTDKDTEITCSERVRTYWIIIELKHKAREKPYDSKSLRTALQKEITTRY 250

EpCAM_aa       175 QLDPKFITSILYENNVITIDLVQNSSQKTQNDVDIADVAYYFEKDVKGES 224
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_aa    251 QLDPKFITSILYENNVITIDLVQNSSQKTQNDVDIADVAYYFEKDVKGES 300

EpCAM_aa       225 LFHSKKMDLTVNGEQLDLDPGQTLIYYVDEKAPEFSMQGLKAGVIAVIVV 274
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr232V3_aa    301 LFHSKKMDLTVNGEQLDLDPGQTLIYYVDEKAPEFSMQGLKAGVIAVIVV 350

EpCAM_aa       275 VVIAVVAGIVVLVISRKKRMAKYEKAEIKEMGEMHRELNA           314
                   ||||||||||||||||||||||||||||||||||||||||
Ovr232V3_aa    351 VVIAVVAGIVVLVISRKKRMAKYEKAEIKEMGEMHRELNA           390
```

FIGURE 9

```
Ovr107          1 AGAGCAAGGAAGGGCAGGGGACCTGGGAAGGAAGTTCTGGAAGGCAGTGG  50

455_051.nt.2    1                                                      0

Ovr107         51 GGTTTGAGATTGGACCCAGGGTCAAGATAGAACATGAAGGTGGGATGAGG 100

455_051.nt.2    1                                                      0

Ovr107        101 ACATGAACAGAACATGGCCAAGAAGGATCTGGGGGAGCAGCCAGGACGAG 150

455_051.nt.2    1                                                      0

Ovr107        151 GCGGAGCTGATCCGAGAGGACATCCAGGGGGCTCTGCACAATTACCGCTC 200

455_051.nt.2    1                                                      0

Ovr107        201 GGGCCGCGGGGAGCGCAGGGCGGCGGCGCTCAGGGCCACGCAGGAGGAGT 250

455_051.nt.2    1                                                      0

Ovr107        251 TGCAGCGCGACCGCTCGCCCGCCGCTGAGACCCCGCCCCTGCAGCGCCGC 300

455_051.nt.2    1                                                      0

Ovr107        301 CCGTCAGTCCGCGCAGTGATCAGCACCGTAGAGCGGGGCGCGGGCCGCGG 350

455_051.nt.2    1                                                      0

Ovr107        351 ACGACCCCAGGCGAAGCCCATTCCCGAGGCAGAGGAGGCGCAGAGGCCTG 400

455_051.nt.2    1                                                0

Ovr107        401 AGCCGGTGGGGACCTCGAGCAA-------CGCTGACTC----GGC-CTCC 438
                            ||.|||...|||       ||||  |||    ||| ||||
455_051.nt.2    1           GATCTCTTCCAAATGTCCCCGCT--CTCCCCAGGCTCTCC  38

Ovr107        439 CCGGACCTGGGTCC---------CCGGGGTCCTGACCTGGCGGTTCTGCA 479
                  ||          |||         ||.|||  |||||||          ||
455_051.nt.2   39 CC---------TCCCGCCACTTGCCAGGG--CTGACCT----------CA  67

Ovr107        480 -GGCGGAGCGGGAAGTGGACATCCTGAACCACGTGTTCGACGACGTAGAG 528
                   .||                |||  ||.||||..||||.|
455_051.nt.2   68 CCGC---------------CAT-CTTAACCGGGTGTCC------------  89

Ovr107        529 AGCTTTGTATCGAGGCTGCAGAAGTCGGCGGAGGCGGCCAGGGTGCTGGA 578
                  |.||.|.|       ||||               |.|||  .|||||||.
455_051.nt.2   90 ACCTCTCT-------CTGC---------------CTGCC-TGGTGCTGGC 116

Ovr107        579 GCACCGGGAACGCGGCCGCAGGAGCCGGCGCCGGGCGGCT----GGGGAG 624
                  .|        ||||.||.|| ..||| |||||.|.|.|||     ...|||
455_051.nt.2  117 CC--------CGCGTCCCCA-TCGCC-GCGCCCGTCTGCTCCCCTCAGAG 156

Ovr107        625 GGCTTGCTGACGCTGCGGGCCAAGCCGCCCTCGGAGGCCGAGTACACCGA 674
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2  157 GGCTTGCTGACGCTGCGGGCCAAGCCGCCCTCGGAGGCCGAGTACACCGA 206

Ovr107        675 CGTGCTGCAGAAGATCAAGTACGCCTTCAGCCTGCTGGCCCGGCTGCGCG 724
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2  207 CGTGCTGCAGAAGATCAAGTACGCCTTCAGCCTGCTGGCCCGGCTGCGCG 256
```

FIGURE 9 (continued)

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Ovr107        725 GCAACATCGCCGACCCCTCCTCTCCGGAGCTGTTGCACTTCCTTTTCGGG 774
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2  257 GCAACATCGCCGACCCCTCCTCTCCGGAGCTGTTGCACTTCCTTTTCGGG 306

Ovr107        775 CCTCTGCAGATGATTGTGAACACGTCGGGGGGGCCGGAGTTCGCGAGCAG 824
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2  307 CCTCTGCAGATGATTGTGAACACGTCGGGGGGGCCGGAGTTCGCGAGCAG 356

Ovr107        825 TGTGCGGCGGCCGCATCTGACATCGGATGCCGTGGCGCTGCTGCGGGACA 874
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2  357 TGTGCGGCGGCCGCATCTGACATCGGATGCCGTGGCGCTGCTGCGGGACA 406

Ovr107        875 ACGTCACTCCACGTGAAAACGAGCTCTGGACCTCGCTGGGGGACTCGTGG 924
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2  407 ACGTCACTCCACGTGAAAACGAGCTCTGGACCTCGCTGGGGGACTCGTGG 456

Ovr107        925 ACCCGCCCCGGGCTGGAGCTGTCCCCGGAGGAGGGACCCCCATACAGACC 974
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2  457 ACCCGCCCCGGGCTGGAGCTGTCCCCGGAGGAGGGACCCCCATACAGACC 506

Ovr107        975 CGAGTTCTTCAGCGGCTGGGAGCCGCCGGTCACTGACCCGCAGAGCCGCG 1024
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2  507 CGAGTTCTTCAGCGGCTGGGAGCCGCCGGTCACTGACCCGCAGAGCCGCG 556

Ovr107       1025 CCTGGGAGGACCCAGTTGAGAAACAGCTACAGCACGAGCGGAGGCGCCGG 1074
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2  557 CCTGGGAGGACCCAGTTGAGAAACAGCTACAGCACGAGCGGAGGCGCCGG 606

Ovr107       1075 CAGCAAAGCGCCCCCCAGGTCGCTGTCAATGGTCACCGAGACTTGGAGCC 1124
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2  607 CAGCAAAGCGCCCCCCAGGTCGCTGTCAATGGTCACCGAGACTTGGAGCC 656

Ovr107       1125 AGAATCTGAGCCTCAGCTGGAGTCAGAGACAGCAGGAAAATGGGTCCTGT 1174
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2  657 AGAATCTGAGCCTCAGCTGGAGTCAGAGACAGCAGGAAAATGGGTCCTGT 706

Ovr107       1175 GTAATTATGACTTCCAGGCCCGCAACAGCAGTGAGCTGTCGGTCAAGCAG 1224
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2  707 GTAATTATGACTTCCAGGCCCGCAACAGCAGTGAGCTGTCGGTCAAGCAG 756

Ovr107       1225 CGGGACGTACTGGAGGTCCTGGATGACAGTCGTAAGTGGTGGAAGGTTCG 1274
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2  757 CGGGACGTACTGGAGGTCCTGGATGACAGTCGTAAGTGGTGGAAGGTTCG 806

Ovr107       1275 GGACCCAGCGGGGCAGGAGGGATATGTGCCCTACAACATCCTGACACCCT 1324
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2  807 GGACCCAGCGGGGCAGGAGGGATATGTGCCCTACAACATCCTGACACCCT 856

Ovr107       1325 ACCCCGGACCCCGGCTGCACCACAGCCAAAGCCCTGCCCGCAGCCTGAAC 1374
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2  857 ACCCCGGACCCCGGCTGCACCACAGCCAAAGCCCTGCCCGCAGCCTGAAC 906

Ovr107       1375 AGCACTCCTCCTCCACCACCAGCCCCAGCCCCGGCCCCACCTCCAGCTCT 1424
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2  907 AGCACTCCTCCTCCACCACCAGCCCCAGCCCCGGCCCCACCTCCAGCTCT 956

Ovr107       1425 GGCTCGGCCCCGCTGGGACAGGCCCCGCTGGGACAGCTGCGATAGCCTCA 1474
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2  957 GGCTCGGCCCCGCTGGGACAGGCCCCGCTGGGACAGCTGCGATAGCCTCA 1006
```

FIGURE 9 (continued)

```
Ovr107          1475  ACGGCTTGGACCCCAGCGAGAAGGAGAAATTCTCCCAGATGCTCATCGTC 1524
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt. 21007     ACGGCTTGGACCCCAGCGAGAAGGAGAAATTCTCCCAGATGCTCATCGTC 1056

Ovr107          1525  AACGAGGAACTGCAGGCGCGCCTGGCCCAGGGCCGCTCGGGACCGAGCCG 1574
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2    1057  AACGAGGAACTGCAGGCGCGCCTGGCCCAGGGCCGCTCGGGACCGAGCCG 1106

Ovr107          1575  CGCAGTCCCAGGGCCCCGCGCCCCGGAACCGCAGCTCAGCCCGGGCTCGG 1624
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2    1107  CGCAGTCCCAGGGCCCCGCGCCCCGGAACCGCAGCTCAGCCCGGGCTCGG 1156

Ovr107          1625  ACGCCTCCGAGGTCCGCGCCTGGCTGCAGGCCAAGGGCTTTAGCTCCGGG 1674
                      ||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2    1157  ACGCCTCCGAGGTCCGCGCCTGGCTGCAGGCCAAGGGCTTTAGCTCCG-- 1204

Ovr107          1675  ACCGTGGACGCGCTGGGTGTGCTGACCGGGGCGCAGCTTTTCTCGCTGCA 1724

455_051.nt.2    1205  -------------------------------------------------- 1204

Ovr107          1725  GAGGGAGGAGCTGCGGGCGGTGAGCCCCGAGGAGGGGGCACGTGTGTACA 1774
                      ||.|||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2    1205  GAAGGAGGAGCTGCGGGCGGTGAGCCCCGAGGAGGGGGCACGTGTGTACA 1254

Ovr107          1775  GCCAGGTCACCGTGCAGCGCTCGCTGCTGGAGGACAAAGAGAAAGTGTCA 1824
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2    1255  GCCAGGTCACCGTGCAGCGCTCGCTGCTGGAGGACAAAGAGAAAGTGTCA 1304

Ovr107          1825  GAGCTGGAGGCAGTGATGGAGAAGCAAAAGAAGAAGGTGGAAGGCGAGGT 1874
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2    1305  GAGCTGGAGGCAGTGATGGAGAAGCAAAAGAAGAAGGTGGAAGGCGAGGT 1354

Ovr107          1875  GGAAATGGAGGTCATTTGACCTGCCAGGCGCCCTTCGCAAAGAGTGACGA 1924
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2    1355  GGAAATGGAGGTCATTTGACCTGCCAGGCGCCCTTCGCAAAGAGTGACGA 1404

Ovr107          1925  GGCCCCGTGGGAGAACGGACTCCTCAGACTCTCCCCAATAGCGGAAGTCG 1974
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2    1405  GGCCCCGTGGGAGAACGGACTCCTCAGACTCTCCCCAATAGCGGAAGTCG 1454

Ovr107          1975  ATCTTCTGAAGGATGGCCAATCTGCTCCGGCCCTGGTCTTCCCCCATCCC 2024
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2    1455  ATCTTCTGAAGGATGGCCAATCTGCTCCGGCCCTGGTCTTCCCCCATCCC 1504

Ovr107          2025  GGTGGACAGACTTAACGATCCTTGCTGCAGTCCCTCCGGAGAGGATCTGG 2074
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2    1505  GGTGGACAGACTTAACGATCCTTGCTGCAGTCCCTCCGGAGAGGATCTGG 1554

Ovr107          2075  ACTGGCTGGGAGTGGGGAGGGCGTGGAGACAGTCTACGGAAAGCGCTAGC 2124
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2    1555  ACTGGCTGGGAGTGGGGAGGGCGTGGAGACAGTCTACGGAAAGCGCTAGC 1604

Ovr107          2125  AGACCCCCGAGAGGGTGCAGTGGAGCCCTGAGCATTGTAATATGCGGCCC 2174
                      ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.2    1605  AGACCCCCGAGAGGGTGCAGTGGAGCCCTGAGCATTGTAATATGCGGCCC 1654

Ovr107          2175  AGCCTATAAACAGCCTCCGTGCTTAGCAAAAAAAAAAAAAAAAAAAA    2221
                      ||||||||||||||||||||||||||||.
455_051.nt.2    1655  AGCCTATAAACAGCCTCCGTGCTTAGCAG                      1683
```

FIGURE 10

```
Ovr107_aa        1 MNRTWPRRIWGSSQDEAELIREDIQGALHNYRSGRGERRAAALRATQEEL  50

455_051.aa.3     1                                                      0

Ovr107_aa       51 QRDRSPAAETPPLQRRPSVRAVISTVERGAGRGRPQAKPIPEAEEAQRPE 100

455_051.aa.3     1                                                      0

Ovr107_aa      101 PVGTSSNADSASPDLGPRGPDLAVLQAEREVDILNHVFDDVESFVSRLQK 150
                             .|| |.|..|...:.:|:               ..:.|..
455_051.aa.3     1           MSP-LSPGSPLPPLARAD---------------LTAILTG  24

Ovr107_aa      151 SAEAARVLEHRERGRRSRRRAAGEGLLTLRAKPPSEAEYTDVLQKIKYAF 200
                   ....:..|....|..|..|....|||||||||||||||||||||||||||
455_051.aa.3    25 CPPLSACLVLAPRPHRRARLLPSEGLLTLRAKPPSEAEYTDVLQKIKYAF  74

Ovr107_aa      201 SLLARLRGNIADPSSPELLHFLFGPLQMIVNTSGGPEFASSVRRPHLTSD 250
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.aa.3    75 SLLARLRGNIADPSSPELLHFLFGPLQMIVNTSGGPEFASSVRRPHLTSD 124

Ovr107_aa      251 AVALLRDNVTPRENELWTSLGDSWTRPGLELSPEEGPPYRPEFFSGWEPP 300
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.aa.3   125 AVALLRDNVTPRENELWTSLGDSWTRPGLELSPEEGPPYRPEFFSGWEPP 174

Ovr107_aa      301 VTDPQSRAWEDPVEKQLQHERRRRQQSAPQVAVNGHRDLEPESEPQLESE 350
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.aa.3   175 VTDPQSRAWEDPVEKQLQHERRRRQQSAPQVAVNGHRDLEPESEPQLESE 224

Ovr107_aa      351 TAGKWVLCNYDFQARNSSELSVKQRDVLEVLDDSRKWWKVRDPAGQEGYV 400
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.aa.3   225 TAGKWVLCNYDFQARNSSELSVKQRDVLEVLDDSRKWWKVRDPAGQEGYV 274

Ovr107_aa      401 PYNILTPYPGPRLHHSQSPARSLNSTPPPPPAPAPAPPPALARPRWDRPR 450
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.aa.3   275 PYNILTPYPGPRLHHSQSPARSLNSTPPPPPAPAPAPPPALARPRWDRPR 324

Ovr107_aa      451 WDSCDSLNGLDPSEKEKFSQMLIVNEELQARLAQGRSGPSRAVPGPRAPE 500
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.aa.3   325 WDSCDSLNGLDPSEKEKFSQMLIVNEELQARLAQGRSGPSRAVPGPRAPE 374

Ovr107_aa      501 PQLSPGSDASEVRAWLQAKGFSSGTVDALGVLTGAQLFSLQREELRAVSP 550
                   |||||||||||||||||||||||||||||||||||||||||:||||||||
455_051.aa.3   375 PQLSPGSDASEVRAWLQAKGFSSGTVDALGVLTGAQLFSLQKEELRAVSP 424

Ovr107_aa      551 EEGARVYSQVTVQRSLLEDKEKVSELEAVMEKQKKKVEGEVEMEVI     596
                   ||||||||||||||||||||||||||||||||||||||||||||||
455_051.aa.3   425 EEGARVYSQVTVQRSLLEDKEKVSELEAVMEKQKKKVEGEVEMEVI     470
```

FIGURE 11

```
Ovr107_aa       1 MNRTWPRRIWGSSQDEAELIREDIQGALHNYRSGRGERRAAALRATQEEL  50

455_051.aa.2    1                                                      0

Ovr107_aa      51 QRDRSPAAETPPLQRRPSVRAVISTVERGAGRGRPQAKPIPEAEEAQRPE 100

455_051.aa.2    1                                                      0

Ovr107_aa     101 PVGTSSNADSASPDLGPRGPDLAVLQAEREVDILNHVFDDVESFVSRLQK  50
                  :....|| |.|..|...:.:|:                  ..:.|..
455_051.aa.2    1 DLFQMSP-LSPGSPLPPLARAD---------------LTAILTG        28

Ovr107_aa     151 SAEAARVLEHRERGRRSRRRAAGEGLLTLRAKPPSEAEYTDVLQKIKYAF 200
                  ....:..|....|..|..|....|||||||||||||||||||||||||||
455_051.aa.2   29 CPPLSACLVLAPRPHRRARLLPSEGLLTLRAKPPSEAEYTDVLQKIKYAF  78

Ovr107_aa     201 SLLARLRGNIADPSSPELLHFLFGPLQMIVNTSGGPEFASSVRRPHLTSD 250
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.aa.2   79 SLLARLRGNIADPSSPELLHFLFGPLQMIVNTSGGPEFASSVRRPHLTSD 128

Ovr107_aa     251 AVALLRDNVTPRENELWTSLGDSWTRPGLELSPEEGPPYRPEFFSGWEPP 300
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.aa.2  129 AVALLRDNVTPRENELWTSLGDSWTRPGLELSPEEGPPYRPEFFSGWEPP 178

Ovr107_aa     301 VTDPQSRAWEDPVEKQLQHERRRRQQSAPQVAVNGHRDLEPESEPQLESE 350
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.aa.2  179 VTDPQSRAWEDPVEKQLQHERRRRQQSAPQVAVNGHRDLEPESEPQLESE 228

Ovr107_aa     351 TAGKWVLCNYDFQARNSSELSVKQRDVLEVLDDSRKWWKVRDPAGQEGYV 400
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.aa.2  229 TAGKWVLCNYDFQARNSSELSVKQRDVLEVLDDSRKWWKVRDPAGQEGYV 278

Ovr107_aa     401 PYNILTPYPGPRLHHSQSPARSLNSTPPPPPAPAPAPPPALARPRWDRPR 450
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.aa.2  279 PYNILTPYPGPRLHHSQSPARSLNSTPPPPPAPAPAPPPALARPRWDRPR 328

Ovr107_aa     451 WDSCDSLNGLDPSEKEKFSQMLIVNEELQARLAQGRSGPSRAVPGPRAPE 500
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.aa.2  329 WDSCDSLNGLDPSEKEKFSQMLIVNEELQARLAQGRSGPSRAVPGPRAPE 378

Ovr107_aa     501 PQLSPGSDASEVRAWLQAKGFSSGTVDALGVLTGAQLFSLQREELRAVSP 550
                  ||||||||||||||||||||||||......
455_051.aa.2  379 PQLSPGSDASEVRAWLQAKGFSSGRRSCGR                     408

Ovr107_aa     551 EEGARVYSQVTVQRSLLEDKEKVSELEAVMEKQKKKVEGEVEMEVI     596

455_051.aa.2  409                                                   408
```

FIGURE 12

```
Ovr107           1 AGAGCAAGGAAGGGCAGGGGACCTGGGAAGGAAGTTCTGGAAGGCAGTGG 50

455_051.nt.3     1                                                    0

Ovr107          51 GGTTTGAGATTGGACCCAGGGTCAAGATAGAACATGAAGGTGGGATGAGG 100

455_051.nt.3     1                                                    0

Ovr107         101 ACATGAACAGAACATGGCCAAGAAGGATCTGGGGGAGCAGCCAGGACGAG 150

455_051.nt.3     1                                                    0

Ovr107         151 GCGGAGCTGATCCGAGAGGACATCCAGGGGGCTCTGCACAATTACCGCTC 200

455_051.nt.3     1                                                    0

Ovr107         201 GGGCCGCGGGGAGCGCAGGGCGGCGGCGCTCAGGGCCACGCAGGAGGAGT 250

455_051.nt.3     1                                                    0

Ovr107         251 TGCAGCGCGACCGCTCGCCCGCCGCTGAGACCCCGCCCCTGCAGCGCCGC 300

455_051.nt.3     1                                                    0

Ovr107         301 CCGTCAGTCCGCGCAGTGATCAGCACCGTAGAGCGGGGCGCGGGCCGCGG 350

455_051.nt.3     1                                                    0

Ovr107         351 ACGACCCCAGGCGAAGCCCATTCCCGAGGCAGAGGAGGCGCAGAGGCCTG 400

455_051.nt.3     1                                                    0

Ovr107         401 AGCCGGTGGGGACCTCGAGCAA-------CGCTGACTC----GGC-CTCC 438
                             ||.|||...|||       ||||  |||    ||| ||||
455_051.nt.3     1           GATCTCTTCCAAATGTCCCCGCT--CTCCCCAGGCTCTCC 38

Ovr107         439 CCGGACCTGGGTCC---------CCGGGGTCCTGACCTGGCGGTTCTGCA 479
                   ||         |||         ||.|||  |||||||          ||
455_051.nt.3    39 CC---------TCCCGCCACTTGCCAGGG--CTGACCT----------CA 67

Ovr107         480 -GGCGGAGCGGGAAGTGGACATCCTGAACCACGTGTTCGACGACGTAGAG 528
                    .||               ||| ||.||||..||||.|
455_051.nt.3    68 CCGC---------------CAT-CTTAACCGGGTGTCC------------ 89

Ovr107         529 AGCTTTGTATCGAGGCTGCAGAAGTCGGCGGAGGCGGCCAGGGTGCTGGA 578
                   |.||.|.|       ||||               |.||| .||||||||.
455_051.nt.3    90 ACCTCTCT-------CTGC---------------CTGCC-TGGTGCTGGC 116

Ovr107         579 GCACCGGGAACGCGGCCGCAGGAGCCGGCGCCGGGCGGCT----GGGGAG 624
                   .|        ||||.||.|| ..||| |||||.|.|.|||    ...|||
455_051.nt.3   117 CC--------CGCGTCCCCA-TCGCC-GCGCCCGTCTGCTCCCCTCAGAG 156

Ovr107         625 GGCTTGCTGACGCTGCGGGCCAAGCCGCCCTCGGAGGCCGAGTACACCGA 674
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3   157 GGCTTGCTGACGCTGCGGGCCAAGCCGCCCTCGGAGGCCGAGTACACCGA 206

Ovr107         675 CGTGCTGCAGAAGATCAAGTACGCCTTCAGCCTGCTGGCCCGGCTGCGCG 724
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3   207 CGTGCTGCAGAAGATCAAGTACGCCTTCAGCCTGCTGGCCCGGCTGCGCG 256
```

FIGURE 12 (continued)

```
Ovr107        725  GCAACATCGCCGACCCCTCCTCTCCGGAGCTGTTGCACTTCCTTTTCGGG  774
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3  257  GCAACATCGCCGACCCCTCCTCTCCGGAGCTGTTGCACTTCCTTTTCGGG  306

Ovr107        775  CCTCTGCAGATGATTGTGAACACGTCGGGGGGGCCGGAGTTCGCGAGCAG  824
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3  307  CCTCTGCAGATGATTGTGAACACGTCGGGGGGGCCGGAGTTCGCGAGCAG  356

Ovr107        825  TGTGCGGCGGCCGCATCTGACATCGGATGCCGTGGCGCTGCTGCGGGACA  874
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3  357  TGTGCGGCGGCCGCATCTGACATCGGATGCCGTGGCGCTGCTGCGGGACA  406

Ovr107        875  ACGTCACTCCACGTGAAAACGAGCTCTGGACCTCGCTGGGGGACTCGTGG  924
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3  407  ACGTCACTCCACGTGAAAACGAGCTCTGGACCTCGCTGGGGGACTCGTGG  456

Ovr107        925  ACCCGCCCCGGGCTGGAGCTGTCCCCGGAGGAGGGACCCCCATACAGACC  974
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3  457  ACCCGCCCCGGGCTGGAGCTGTCCCCGGAGGAGGGACCCCCATACAGACC  506

Ovr107        975  CGAGTTCTTCAGCGGCTGGGAGCCGCCGGTCACTGACCCGCAGAGCCGCG  024
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3  507  CGAGTTCTTCAGCGGCTGGGAGCCGCCGGTCACTGACCCGCAGAGCCGCG  556

Ovr107       1025  CCTGGGAGGACCCAGTTGAGAAACAGCTACAGCACGAGCGGAGGCGCCGG  1074
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3  557  CCTGGGAGGACCCAGTTGAGAAACAGCTACAGCACGAGCGGAGGCGCCGG  606

Ovr107       1075  CAGCAAAGCGCCCCCCAGGTCGCTGTCAATGGTCACCGAGACTTGGAGCC  1124
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3  607  CAGCAAAGCGCCCCCCAGGTCGCTGTCAATGGTCACCGAGACTTGGAGCC  656

Ovr107       1125  AGAATCTGAGCCTCAGCTGGAGTCAGAGACAGCAGGAAAATGGGTCCTGT  1174
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3  657  AGAATCTGAGCCTCAGCTGGAGTCAGAGACAGCAGGAAAATGGGTCCTGT  706

Ovr107       1175  GTAATTATGACTTCCAGGCCCGCAACAGCAGTGAGCTGTCGGTCAAGCAG  1224
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3  707  GTAATTATGACTTCCAGGCCCGCAACAGCAGTGAGCTGTCGGTCAAGCAG  756

Ovr107       1225  CGGGACGTACTGGAGGTCCTGGATGACAGTCGTAAGTGGTGGAAGGTTCG  1274
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3  757  CGGGACGTACTGGAGGTCCTGGATGACAGTCGTAAGTGGTGGAAGGTTCG  806

Ovr107       1275  GGACCCAGCGGGGCAGGAGGGATATGTGCCCTACAACATCCTGACACCCT  1324
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3  807  GGACCCAGCGGGGCAGGAGGGATATGTGCCCTACAACATCCTGACACCCT  856

Ovr107       1325  ACCCCGGACCCCGGCTGCACCACAGCCAAAGCCCTGCCCGCAGCCTGAAC  374
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3  857  ACCCCGGACCCCGGCTGCACCACAGCCAAAGCCCTGCCCGCAGCCTGAAC  906

Ovr107       1375  AGCACTCCTCCTCCACCACCAGCCCCAGCCCCGGCCCCACCTCCAGCTCT  1424
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3  907  AGCACTCCTCCTCCACCACCAGCCCCAGCCCCGGCCCCACCTCCAGCTCT  956

Ovr107       1425  GGCTCGGCCCCGCTGGGACAGGCCCCGCTGGGACAGCTGCGATAGCCTCA  1474
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3  957  GGCTCGGCCCCGCTGGGACAGGCCCCGCTGGGACAGCTGCGATAGCCTCA  1006
```

FIGURE 12 (continued)

```
Ovr107       1475 ACGGCTTGGACCCCAGCGAGAAGGAGAAATTCTCCCAGATGCTCATCGTC 1524
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3 1007 ACGGCTTGGACCCCAGCGAGAAGGAGAAATTCTCCCAGATGCTCATCGTC 1056

Ovr107       1525 AACGAGGAACTGCAGGCGCGCCTGGCCCAGGGCCGCTCGGGACCGAGCCG 1574
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3 1057 AACGAGGAACTGCAGGCGCGCCTGGCCCAGGGCCGCTCGGGACCGAGCCG 1106

Ovr107       1575 CGCAGTCCCAGGGCCCCGCGCCCCGGAACCGCAGCTCAGCCCGGGCTCGG 1624
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3 1107 CGCAGTCCCAGGGCCCCGCGCCCCGGAACCGCAGCTCAGCCCGGGCTCGG 1156

Ovr107       1625 ACGCCTCCGAGGTCCGCGCCTGGCTGCAGGCCAAGGGCTTTAGCTCCGGG 1674
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3 1157 ACGCCTCCGAGGTCCGCGCCTGGCTGCAGGCCAAGGGCTTTAGCTCCGGG 1206

Ovr107       1675 ACCGTGGACGCGCTGGGTGTGCTGACCGGGGCGCAGCTTTTCTCGCTGCA 1724
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3 1207 ACCGTGGACGCGCTGGGTGTGCTGACCGGGGCGCAGCTTTTCTCGCTGCA 1256

Ovr107       1725 GAGGGAGGAGCTGCGGGCGGTGAGCCCCGAGGAGGGGGCACGTGTGTACA 1774
                  ||.|||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3 1257 GAAGGAGGAGCTGCGGGCGGTGAGCCCCGAGGAGGGGGCACGTGTGTACA 1306

Ovr107       1775 GCCAGGTCACCGTGCAGCGCTCGCTGCTGGAGGACAAAGAGAAAGTGTCA 1824
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3 1307 GCCAGGTCACCGTGCAGCGCTCGCTGCTGGAGGACAAAGAGAAAGTGTCA 1356

Ovr107       1825 GAGCTGGAGGCAGTGATGGAGAAGCAAAAGAAGAAGGTGGAAGGCGAGGT 1874
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3 1357 GAGCTGGAGGCAGTGATGGAGAAGCAAAAGAAGAAGGTGGAAGGCGAGGT 1406

Ovr107       1875 GGAAATGGAGGTCATTTGACCTGCCAGGCGCCCTTCGCAAAGAGTGACGA 1924
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3 1407 GGAAATGGAGGTCATTTGACCTGCCAGGCGCCCTTCGCAAAGAGTGACGA 1456

Ovr107       1925 GGCCCCGTGGGAGAACGGACTCCTCAGACTCTCCCCAATAGCGGAAGTCG 1974
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3 1457 GGCCCCGTGGGAGAACGGACTCCTCAGACTCTCCCCAATAGCGGAAGTCG 1506

Ovr107       1975 ATCTTCTGAAGGATGGCCAATCTGCTCCGGCCCTGGTCTTCCCCCATCCC 2024
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3 1507 ATCTTCTGAAGGATGGCCAATCTGCTCCGGCCCTGGTCTTCCCCCATCCC 1556

Ovr107       2025 GGTGGACAGACTTAACGATCCTTGCTGCAGTCCCTCCGGAGAGGATCTGG 2074
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3 1557 GGTGGACAGACTTAACGATCCTTGCTGCAGTCCCTCCGGAGAGGATCTGG 1606

Ovr107       2075 ACTGGCTGGGAGTGGGGAGGGCGTGGAGACAGTCTACGGAAAGCGCTAGC 2124
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3 1607 ACTGGCTGGGAGTGGGGAGGGCGTGGAGACAGTCTACGGAAAGCGCTAGC 1656

Ovr107       2125 AGACCCCCGAGAGGGTGCAGTGGAGCCCTGAGCATTGTAATATGCGGCCC 2174
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.3 1657 AGACCCCCGAGAGGGTGCAGTGGAGCCCTGAGCATTGTAATATGCGGCCC 1706

Ovr107       2175 AGCCTATAAACAGCCTCCGTGCTTAGCAAAAAAAAAAAAAAAAAAAA    2221
                  ||||||||||||||||||||||||||||.
455_051.nt.3 1707 AGCCTATAAACAGCCTCCGTGCTTAGCAG                      1735
```

FIGURE 13

```
Ovr107          1 AGAGCAAGGAAGGGCAGGGGACCTGGGAAGGAAGTTCTGGAAGGCAGTGG   50

455_051.nt.4    1                                                       0

Ovr107         51 GGTTTGAGATTGGACCCAGGGTCAAGATAGAACATGAAGGTGGGATGAGG  100

455_051.nt.4    1                                                       0

Ovr107        101 ACATGAACAGAACATGGCCAAGAAGGATCTGGGGGAGCAGCCAGGACGAG  150

455_051.nt.4    1                                                       0

Ovr107        151 GCGGAGCTGATCCGAGAGGACATCCAGGGGGCTCTGCACAATTACCGCTC  200

455_051.nt.4    1                                                       0

Ovr107        201 GGGCCGCGGGGAGCGCAGGGCGGCGGCGCTCAGGGCCACGCAGGAGGAGT  250

455_051.nt.4    1                                                       0

Ovr107        251 TGCAGCGCGACCGCTCGCCCGCCGCTGAGACCCCGCCCCTGCAGCGCCGC  300

455_051.nt.4    1                                                       0

Ovr107        301 CCGTCAGTCCGCGCAGTGATCAGCACCGTAGAGCGGGGCGCGGGCCGCGG  350

455_051.nt.4    1                                                       0

Ovr107        351 ACGACCCCAGGCGAAGCCCATTCCCGAGGCAGAGGAGGCGCAGAGGCCTG  400

455_051.nt.4    1                                                       0

Ovr107        401 AGCCGGTGGGGACCTCGAGCAA-------CGCTGACTC----GGC-CTCC  438
                            ||.|||...|||       ||||  |||    ||| ||||
455_051.nt.4    1           GATCTCTTCCAAATGTCCCCGCT--CTCCCCAGGCTCTCC   38

Ovr107        439 CCGGACCTGGGTCC---------CCGGGGTCCTGACCTGGCGGTTCTGCA   79
                  ||         |||         ||.|||  |||||||          ||
455_051.nt.4   39 CC---------TCCCGCCACTTGCCAGGG--CTGACCT----------CA   67

Ovr107        480 -GGCGGAGCGGGAAGTGGACATCCTGAACCACGTGTTCGACGACGTAGAG   28
                   .||               ||| ||.||||..||||.|
455_051.nt.4   68 CCGC---------------CAT-CTTAACCGGGTGTCC------------   89

Ovr107        529 AGCTTTGTATCGAGGCTGCAGAAGTCGGCGGAGGCGGCCAGGGTGCTGGA   78
                  |.||.|.|       ||||               |.||| .||||||||.
455_051.nt.4   90 ACCTCTCT-------CTGC---------------CTGCC-TGGTGCTGGC   16

Ovr107        579 GCACCGGGAACGCGGCCGCAGGAGCCGGCGCCGGGCGGCT----GGGGAG   24
                  .|        ||||.||.|| ..||| |||||.|.|.|||    ...|||
455_051.nt.4  117 CC--------CGCGTCCCCA-TCGCC-GCGCCCGTCTGCTCCCCTCAGAG  156

Ovr107        625 GGCTTGCTGACGCTGCGGGCCAAGCCGCCCTCGGAGGCCGAGTACACCGA  674
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4  157 GGCTTGCTGACGCTGCGGGCCAAGCCGCCCTCGGAGGCCGAGTACACCGA  206

Ovr107        675 CGTGCTGCAGAAGATCAAGTACGCCTTCAGCCTGCTGGCCCGGCTGCGCG  724
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4  207 CGTGCTGCAGAAGATCAAGTACGCCTTCAGCCTGCTGGCCCGGCTGCGCG  256
```

FIGURE 13 (continued)

```
Ovr107        725  GCAACATCGCCGACCCCTCCTCTCCGGAGCTGTTGCACTTCCTTTTCGGG  774
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4  257  GCAACATCGCCGACCCCTCCTCTCCGGAGCTGTTGCACTTCCTTTTCGGG  306

Ovr107        775  CCTCTGCAGATGATTGTGAACACGTCGGGGGGGCCGGAGTTCGCGAGCA   824
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4  307  CCTCTGCAGATGATTGTGAACACGTCGGGGGGGCCGGAGTTCGCGAGCAG  356

Ovr107        825  TGTGCGGCGGCCGCATCTGACATCGGATGCCGTGGCGCTGCTGCGGGACA  874
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4  357  TGTGCGGCGGCCGCATCTGACATCGGATGCCGTGGCGCTGCTGCGGGACA  406

Ovr107        875  ACGTCACTCCACGTGAAAACGAGCTCTGGACCTCGCTGGGGGACTCGTGG  924
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4  407  ACGTCACTCCACGTGAAAACGAGCTCTGGACCTCGCTGGGGGACTCGTGG  456

Ovr107        925  ACCCGCCCCGGGCTGGAGCTGTCCCCGGAGGAGGGACCCCCATACAGACC  974
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4  457  ACCCGCCCCGGGCTGGAGCTGTCCCCGGAGGAGGGACCCCCATACAGACC  506

Ovr107        975  CGAGTTCTTCAGCGGCTGGGAGCCGCCGGTCACTGACCCGCAGAGCCGCG  1024
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4  507  CGAGTTCTTCAGCGGCTGGGAGCCGCCGGTCACTGACCCGCAGAGCCGCG  556

Ovr107        1025 CCTGGGAGGACCCAGTTGAGAAACAGCTACAGCACGAGCGGAGGCGCCGG  1074
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4  557  CCTGGGAGGACCCAGTTGAGAAACAGCTACAGCACGAGCGGAGGCGCCGG  606

Ovr107        1075 CAGCAAAGCGCCCCCCAGGTCGCTGTCAATGGTCACCGAGACTTGGAGCC  1124
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4  607  CAGCAAAGCGCCCCCCAGGTCGCTGTCAATGGTCACCGAGACTTGGAGCC  656

Ovr107        1125 AGAATCTGAGCCTCAGCTGGAGTCAGAGACAGCAGGAAAATGGGTCCTGT  1174
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4  657  AGAATCTGAGCCTCAGCTGGAGTCAGAGACAGCAGGAAAATGGGTCCTGT  706

Ovr107        1175 GTAATTATGACTTCCAGGCCCGCAACAGCAGTGAGCTGTCGGTCAAGCAG  224
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4  707  GTAATTATGACTTCCAGGCCCGCAACAGCAGTGAGCTGTCGGTCAAGCAG  756

Ovr107        1225 CGGGACGTACTGGAGGTCCTGGATGACAGTCGTAAGTGGTGGAAGGTTCG  1274
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4  757  CGGGACGTACTGGAGGTCCTGGATGACAGTCGTAAGTGGTGGAAGGTTCG  806

Ovr107        1275 GGACCCAGCGGGGCAGGAGGGATATGTGCCCTACAACATCCTGACACCCT  1324
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4  807  GGACCCAGCGGGGCAGGAGGGATATGTGCCCTACAACATCCTGACACCCT  856

Ovr107        1325 ACCCCGGACCCCGGCTGCACCACAGCCAAAGCCCTGCCCGCAGCCTGAAC  1374
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4  857  ACCCCGGACCCCGGCTGCACCACAGCCAAAGCCCTGCCCGCAGCCTGAAC  906

Ovr107        1375 AGCACTCCTCCTCCACCACCAGCCCCAGCCCCGGCCCCACCTCCAGCTCT  1424
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4  907  AGCACTCCTCCTCCACCACCAGCCCCAGCCCCGGCCCCACCTCCAGCTCT  956

Ovr107        1425 GGCTCGGCCCCGCTGGGACAGGCCCCGCTGGGACAGCTGCGATAGCCTCA  1474
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4  957  GGCTCGGCCCCGCTGGGACAGGCCCCGCTGGGACAGCTGCGATAGCCTCA  1006
```

FIGURE 13 (continued)

```
Ovr107         1475 ACGGCTTGGACCCCAGCGAGAAGGAGAAATTCTCCCAGATGCTCATCGTC 1524
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4   1007 ACGGCTTGGACCCCAGCGAGAAGGAGAAATTCTCCCAGATGCTCATCGTC 1056

Ovr107         1525 AACGAGGAACTGCAGGCGCGCCTGGCCCAGGGCCGCTCGGGACCGAGCCG 1574
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4   1057 AACGAGGAACTGCAGGCGCGCCTGGCCCAGGGCCGCTCGGGACCGAGCCG 1106

Ovr107         1575 CGCAGTCCCAGGGCCCCGCGCCCCGGAACCGCAGCTCAGCCCGGGCTCGG 1624
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4   1107 CGCAGTCCCAGGGCCCCGCGCCCCGGAACCGCAGCTCAGCCCGGGCTCGG 1156

Ovr107         1625 ACGCCTCCGAGGTCCGCGCCTGGCTGCAGGCCAAGGGCTTTAGCTCCGGG 1674
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4   1157 ACGCCTCCGAGGTCCGCGCCTGGCTGCAGGCCAAGGGCTTTAGCTCCGGG 1206

Ovr107         1675 ACCGTGGACGCGCTGGGTGTGCTGACCGGGGCGCAGCTTTTCTCGCTGCA 1724
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4   1207 ACCGTGGACGCGCTGGGTGTGCTGACCGGGGCGCAGCTTTTCTCGCTGCA 1256

Ovr107         1725 GAGGGAGGAGCTGCGGGCGGTGAGCCCCGAGGAGGGGGCACGTGTGTACA 1774
                    ||.|||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4   1257 GAAGGAGGAGCTGCGGGCGGTGAGCCCCGAGGAGGGGGCACGTGTGTACA 1306

Ovr107         1775 GCCAGGTCACCGTGCAGCGCTCGCTGCTGGAGGACAAAGAGAAAGTGTCA 1824
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4   1307 GCCAGGTCACCGTGCAGCGCTCGCTGCTGGAGGACAAAGAGAAAGTGTCA 1356

Ovr107         1825 GAGCTGGAGGCAGTGATGGAGAAGCAAAAGAAGAAGGTGGAAGGCGAGGT 1874
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4   1357 GAGCTGGAGGCAGTGATGGAGAAGCAAAAGAAGAAGGTGGAAGGCGAGGT 1406

Ovr107         1875 GGAAATGGAGGTCATTTGACCTGCCAGGCGCCCTTCGCAAAGAGTGACGA 1924
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4   1407 GGAAATGGAGGTCATTTGACCTGCCAGGCGCCCTTCGCAAAGAGTGACGA 1456

Ovr107         1925 GGCCCCGTGGGAGAACGGACTCCTCAGACTCTCCCCAATAGCGGAAGTCG 1974
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4   1457 GGCCCCGTGGGAGAACGGACTCCTCAGACTCTCCCCAATAGCGGAAGTCG 1506

Ovr107         1975 ATCTTCTGAAGGATGGCCAATCTGCTCCGGCCCTGGTCTTCCCCCATCCC 2024
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4   1507 ATCTTCTGAAGGATGGCCAATCTGCTCCGGCCCTGGTCTTCCCCCATCCC 1556

Ovr107         2025 GGTGGACAGACTTAACGATCCTTGCTGCAGTCCCTCCGGAGAGGATCTGG 2074
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4   1557 GGTGGACAGACTTAACGATCCTTGCTGCAGTCCCTCCGGAGAGGATCTGG 1606

Ovr107         2075 ACTGGCTGGGAGTGGGGAGGGCGTGGAGACAGTCTACGGAAAGCGCTAGC 2124
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4   1607 ACTGGCTGGGAGTGGGGAGGGCGTGGAGACAGTCTACGGAAAGCGCTAGC 1656

Ovr107         2125 AGACCCCCGAGAGGGTGCAGTGGAGCCCTGAGCATTGTAATATGCGGCCC 2174
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.4   1657 AGACCCCCGAGAGGGTGCAGTGGAGCCCTGAGCATTGTAATATGCGGCCC 1706

Ovr107         2175 AGCCTATAAACAGCCTCCGTGCTTAGCAAAAAAAAAAAAAAAAAAAA    2221
                    ||||||||||||||||||||||||||||.||||||||||||||||||
455_051.nt.4   1707 AGCCTATAAACAGCCTCCGTGCTTAGCAGAAAAAAAAAAAAAAAAAAAAA 1756
```

FIGURE 13 (continued)

```
Ovr107          2222                                                    2221

455_051.nt.4 1757 AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAACATACAAAAAATAAAAGA 1806

Ovr107       2222                                                    2221

455_051.nt.4 1807 ATAGTCAACAAACAAAATAAGAAACTATAGATAATATAAAAATGAAAATA 1856

Ovr107       2222                                                    2221

455_051.nt.4 1857 AAAAAGAGATGGGGTGGGGCCCTTGTCTTTACTCTCTCCCTCTGGAGTGG 1906

Ovr107       2222                                                    2221

455_051.nt.4 1907 GCACACTATATTATTTCGCCCTCCCCCTCTTTTTTTGTATGAGAGGGCTC 1956

Ovr107       2222                                                    2221

455_051.nt.4 1957 TTTTA                                              1961
```

FIGURE 14

```
Ovr107          1 AGAGCAAGGAAGGGCAGGGGACCTGGGAAGGAAGTTCTGGAAGGCAGTGG  50

455_051.nt.5    1                                                     0

Ovr107         51 GGTTTGAGATTGGACCCAGGGTCAAGATAGAACATGAAGGTGGGATGAGG 100

455_051.nt.5    1                                                     0

Ovr107        101 ACATGAACAGAACATGGCCAAGAAGGATCTGGGGGAGCAGCCAGGACGAG 150

455_051.nt.5    1                                                     0

Ovr107        151 GCGGAGCTGATCCGAGAGGACATCCAGGGGGCTCTGCACAATTACCGCTC 200

455_051.nt.5    1                                                     0

Ovr107        201 GGGCCGCGGGGAGCGCAGGGCGGCGGCGCTCAGGGCCACGCAGGAGGAGT 250

455_051.nt.5    1                                                     0

Ovr107        251 TGCAGCGCGACCGCTCGCCCGCCGCTGAGACCCCGCCCCTGCAGCGCCGC 300

455_051.nt.5    1                                                     0

Ovr107        301 CCGTCAGTCCGCGCAGTGATCAGCACCGTAGAGCGGGGCGCGGGCCGCGG  50

455_051.nt.5    1                                                     0

Ovr107        351 ACGACCCCAGGCGAAGCCCATTCCCGAGGCAGAGGAGGCGCAGAGGCCTG 400

455_051.nt.5    1                                                     0

Ovr107        401 AGCCGGTGGGGACCTCGAGCAA-------CGCTGACTC----GGC-CTCC 438
                            ||.|||...|||         ||||  |||    ||| ||||
455_051.nt.5    1           GATCTCTTCCAAATGTCCCCGCT--CTCCCCAGGCTCTCC  38

Ovr107        439 CCGGACCTGGGTCC---------CCGGGGTCCTGACCTGGCGGTTCTGCA  79
                  ||         |||         ||.|||  ||||||          ||
455_051.nt.5   39 CC---------TCCCGCCACTTGCCAGGG--CTGACCT----------CA  67

Ovr107        480 -GGCGGAGCGGGAAGTGGACATCCTGAACCACGTGTTCGACGACGTAGAG 528
                   .||                ||| ||.||||..||||.|
455_051.nt.5   68 CCGC---------------CAT-CTTAACCGGGTGTCC------------  89

Ovr107        529 AGCTTTGTATCGAGGCTGCAGAAGTCGGCGGAGGCGGCCAGGGTGCTGGA 578
                  |.||.|.|       ||||               |.||| .||||||||.
455_051.nt.5   90 ACCTCTCT-------CTGC---------------CTGCC-TGGTGCTGGC  16

Ovr107        579 GCACCGGGAACGCGGCCGCAGGAGCCGGCGCCGGGCGGCT----GGGGAG 624
                  .|        ||||.||.|| ..||| |||||.|.|.|||    ...|||
455_051.nt.5  117 CC--------CGCGTCCCCA-TCGCC-GCGCCCGTCTGCTCCCCTCAGAG 156

Ovr107        625 GGCTTGCTGACGCTGCGGGCCAAGCCGCCCTCGGAGGCCGAGTACACCGA 674
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5  157 GGCTTGCTGACGCTGCGGGCCAAGCCGCCCTCGGAGGCCGAGTACACCGA 206

Ovr107        675 CGTGCTGCAGAAGATCAAGTACGCCTTCAGCCTGCTGGCCCGGCTGCGCG 724
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5  207 CGTGCTGCAGAAGATCAAGTACGCCTTCAGCCTGCTGGCCCGGCTGCGCG 256
```

FIGURE 14 (continued)

```
Ovr107          725 GCAACATCGCCGACCCCTCCTCTCCGGAGCTGTTGCACTTCCTTTTCGGG  774
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5    257 GCAACATCGCCGACCCCTCCTCTCCGGAGCTGTTGCACTTCCTTTTCGGG  306

Ovr107          775 CCTCTGCAGATGATTGTGAACACGTCGGGGGGGCCGGAGTTCGCGAGCAG  824
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5    307 CCTCTGCAGATGATTGTGAACACGTCGGGGGGGCCGGAGTTCGCGAGCAG  356

Ovr107          825 TGTGCGGCGGCCGCATCTGACATCGGATGCCGTGGCGCTGCTGCGGGACA  874
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5    357 TGTGCGGCGGCCGCATCTGACATCGGATGCCGTGGCGCTGCTGCGGGACA  406

Ovr107          875 ACGTCACTCCACGTGAAAACGAGCTCTGGACCTCGCTGGGGGACTCGTGG  924
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5    407 ACGTCACTCCACGTGAAAACGAGCTCTGGACCTCGCTGGGGGACTCGTGG  456

Ovr107          925 ACCCGCCCCGGGCTGGAGCTGTCCCCGGAGGAGGGACCCCCATACAGACC  974
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5    457 ACCCGCCCCGGGCTGGAGCTGTCCCCGGAGGAGGGACCCCCATACAGACC  506

Ovr107          975 CGAGTTCTTCAGCGGCTGGGAGCCGCCGGTCACTGACCCGCAGAGCCGCG  024
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5    507 CGAGTTCTTCAGCGGCTGGGAGCCGCCGGTCACTGACCCGCAGAGCCGCG  556

Ovr107         1025 CCTGGGAGGACCCAGTTGAGAAACAGCTACAGCACGAGCGGAGGCGCCGG 1074
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5    557 CCTGGGAGGACCCAGTTGAGAAACAGCTACAGCACGAGCGGAGGCGCCGG  606

Ovr107         1075 CAGCAAAGCGCCCCCCAGGTCGCTGTCAATGGTCACCGAGACTTGGAGCC 1124
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5    607 CAGCAAAGCGCCCCCCAGGTCGCTGTCAATGGTCACCGAGACTTGGAGCC  656

Ovr107         1125 AGAATCTGAGCCTCAGCTGGAGTCAGAGACAGCAGGAAAATGGGTCCTGT 1174
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5    657 AGAATCTGAGCCTCAGCTGGAGTCAGAGACAGCAGGAAAATGGGTCCTGT  706

Ovr107         1175 GTAATTATGACTTCCAGGCCCGCAACAGCAGTGAGCTGTCGGTCAAGCAG 1224
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5    707 GTAATTATGACTTCCAGGCCCGCAACAGCAGTGAGCTGTCGGTCAAGCAG  756

Ovr107         1225 CGGGACGTACTGGAGGTCCTGGATGACAGTCGTAAGTGGTGGAAGGTTCG 1274
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5    757 CGGGACGTACTGGAGGTCCTGGATGACAGTCGTAAGTGGTGGAAGGTTCG  806

Ovr107         1275 GGACCCAGCGGGGCAGGAGGGATATGTGCCCTACAACATCCTGACACCCT 1324
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5    807 GGACCCAGCGGGGCAGGAGGGATATGTGCCCTACAACATCCTGACACCCT  856

Ovr107         1325 ACCCCGGACCCCGGCTGCACCACAGCCAAAGCCCTGCCCGCAGCCTGAAC 1374
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5    857 ACCCCGGACCCCGGCTGCACCACAGCCAAAGCCCTGCCCGCAGCCTGAAC  906

Ovr107         1375 AGCACTCCTCCTCCACCACCAGCCCCAGCCCCGGCCCCACCTCCAGCTCT 1424
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5    907 AGCACTCCTCCTCCACCACCAGCCCCAGCCCCGGCCCCACCTCCAGCTCT  956

Ovr107         1425 GGCTCGGCCCCGCTGGGACAGGCCCCGCTGGGACAGCTGCGATAGCCTCA 1474
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5    957 GGCTCGGCCCCGCTGGGACAGGCCCCGCTGGGACAGCTGCGATAGCCTCA 1006
```

FIGURE 14 (continued)

```
Ovr107        1475 ACGGCTTGGACCCCAGCGAGAAGGAGAAATTCTCCCAGATGCTCATCGTC 1524
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5  1007 ACGGCTTGGACCCCAGCGAGAAGGAGAAATTCTCCCAGATGCTCATCGTC 1056

Ovr107        1525 AACGAGGAACTGCAGGCGCGCCTGGCCCAGGGCCGCTCGGGACCGAGCCG 1574
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5  1057 AACGAGGAACTGCAGGCGCGCCTGGCCCAGGGCCGCTCGGGACCGAGCCG 1106

Ovr107        1575 CGCAGTCCCAGGGCCCCGCGCCCCGGAACCGCAGCTCAGCCCGGGCTCGG 1624
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5  1107 CGCAGTCCCAGGGCCCCGCGCCCCGGAACCGCAGCTCAGCCCGGGCTCGG 1156

Ovr107        1625 ACGCCTCCGAGGTCCGCGCCTGGCTGCAGGCCAAGGGCTTTAGCTCCGGG 1674
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5  1157 ACGCCTCCGAGGTCCGCGCCTGGCTGCAGGCCAAGGGCTTTAGCTCCGGG 1206

Ovr107        1675 ACCGTGGACGCGCTGGGTGTGCTGACCGGGGCGCAGCTTTTCTCGCTGCA 1724
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5  1207 ACCGTGGACGCGCTGGGTGTGCTGACCGGGGCGCAGCTTTTCTCGCTGCA 1256

Ovr107        1725 GAGGGAGGAGCTGCGGGCGGTGAGCCCCGAGGAGGGGGCACGTGTGTACA 1774
                   ||.|||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5  1257 GAAGGAGGAGCTGCGGGCGGTGAGCCCCGAGGAGGGGGCACGTGTGTACA 1306

Ovr107        1775 GCCAGGTCACCGTGCAGCGCTCGCTGCTGGAGGACAAAGAGAAAGTGTCA 1824
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5  1307 GCCAGGTCACCGTGCAGCGCTCGCTGCTGGAGGACAAAGAGAAAGTGTCA 1356

Ovr107        1825 GAGCTGGAGGCAGTGATGGAGAAGCAAAAGAAGAAGGTGGAAGGCGAGGT 1874
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5  1357 GAGCTGGAGGCAGTGATGGAGAAGCAAAAGAAGAAGGTGGAAGGCGAGGT 1406

Ovr107        1875 GGAAATGGAGGTCATTTGACCTGCCAGGCGCCCTTCGCAAAGAGTGACGA 1924
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5  1407 GGAAATGGAGGTCATTTGACCTGCCAGGCGCCCTTCGCAAAGAGTGACGA 1456

Ovr107        1925 GGCCCCGTGGGAGAACGGACTCCTCAGACTCTCCCCAATAGCGGAAGTCG 1974
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5  1457 GGCCCCGTGGGAGAACGGACTCCTCAGACTCTCCCCAATAGCGGAAGTCG 1506

Ovr107        1975 ATCTTCTGAAGGATGGCCAATCTGCTCCGGCCCTGGTCTTCCCCCATCCC 2024
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5  1507 ATCTTCTGAAGGATGGCCAATCTGCTCCGGCCCTGGTCTTCCCCCATCCC 1556

Ovr107        2025 GGTGGACAGACTTAACGATCCTTGCTGCAGTCCCTCCGGAGAGGATCTGG 2074
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5  1557 GGTGGACAGACTTAACGATCCTTGCTGCAGTCCCTCCGGAGAGGATCTGG 1606

Ovr107        2075 ACTGGCTGGGAGTGGGGAGGGCGTGGAGACAGTCTACGGAAAGCGCTAGC 2124
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5  1607 ACTGGCTGGGAGTGGGGAGGGCGTGGAGACAGTCTACGGAAAGCGCTAGC 1656

Ovr107        2125 AGACCCCCGAGAGGGTGCAGTGGAGCCCTGAGCATTGTAATATGCGGCCC 2174
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.5  1657 AGACCCCCGAGAGGGTGCAGTGGAGCCCTGAGCATTGTAATATGCGGCCC 1706

Ovr107        2175 AGCCTATAAACAGCCTCCGTGCTTAGCAAAAAAAAAAAAAA--------- 2215
                   |||||||||||||||||||||||||||.|||||.||||.|
455_051.nt.5  1707 AGCCTATAAACAGCCTCCGTGCTTAGCAGAAAAASAAAACACATCAACCC 1756
```

FIGURE 14 (continued)

```
Ovr107        2216 AAAAAA                                               2221
                   ||.|||
455_051.nt.5  1757 AACAAACGTTTGGGGTATTCCATGGCCAATACCGTTGTTCCCGTGTGTGA 1806

Ovr107        2222                                                      2221

455_051.nt.5  1807 ACATTGTTATTTCAGCTCACATTTCCCACAGTATTGGAACAACACATCAT 1856

Ovr107        2222                                                      2221

455_051.nt.5  1857 ACCACACACACACAGAACCAATCGAGATATATAAACCCAATGCACACTCA 1906

Ovr107        2222                                                      2221

455_051.nt.5  1907 AACACCTAAT                                           1916
```

FIGURE 15

```
Ovr107             1 AGAGCAAGGAAGGGCAGGGGACCTGGGAAGGAAGTTCTGGAAGGCAGTGG  50

455_051.nt.6       1                                                     0

Ovr107            51 GGTTTGAGATTGGACCCAGGGTCAAGATAGAACATGAAGGTGGGATGAGG 100

455_051.nt.6       1                                                     0

Ovr107           101 ACATGAACAGAACATGGCCAAGAAGGATCTGGGGGAGCAGCCAGGACGAG  50

455_051.nt.6       1                                                     0

Ovr107           151 GCGGAGCTGATCCGAGAGGACATCCAGGGGGCTCTGCACAATTACCGCTC 200

455_051.nt.6       1                                                     0

Ovr107           201 GGGCCGCGGGGAGCGCAGGGCGGCGGCGCTCAGGGCCACGCAGGAGGAGT 250

455_051.nt.6       1                                                     0

Ovr107           251 TGCAGCGCGACCGCTCGCCCGCCGCTGAGACCCCGCCCCTGCAGCGCCGC 300

455_051.nt.6       1                                                     0

Ovr107           301 CCGTCAGTCCGCGCAGTGATCAGCACCGTAGAGCGGGGCGCGGGCCGCGG 350

455_051.nt.6       1                                                     0

Ovr107           351 ACGACCCCAGGCGAAGCCCATTCCCGAGGCAGAGGAGGCGCAGAGGCCTG 400

455_051.nt.6       1                                                     0

Ovr107           401 AGCCGGTGGGACCTCGAGCAA-------CGCTGACTC----GGC-CTCC 438
                               ||.|||...|||       ||||  |||    ||| ||||
455_051.nt.6       1           GATCTCTTCCAAATGTCCCCGCT--CTCCCCAGGCTCTCC  38

Ovr107           439 CCGGACCTGGGTCC---------CCGGGGTCCTGACCTGGCGGTTCTGCA 479
                     ||         |||         ||.|||  |||||||          ||
455_051.nt.6      39 CC---------TCCCGCCACTTGCCAGGG--CTGACCT----------CA  67

Ovr107           480 -GGCGGAGCGGGAAGTGGACATCCTGAACCACGTGTTCGACGACGTAGAG 528
                      .||               ||| ||.||||..||||.|
455_051.nt.6      68 CCGC---------------CAT-CTTAACCGGGTGTCC------------  89

Ovr107           529 AGCTTTGTATCGAGGCTGCAGAAGTCGGCGGAGGCGGCCAGGGTGCTGGA 578
                     |.||.|.|       ||||               |.||| .||||||||.
455_051.nt.6      90 ACCTCTCT-------CTGC---------------CTGCC-TGGTGCTGGC 116

Ovr107           579 GCACCGGGAACGCGGCCGCAGGAGCCGGCGCCGGGCGGCT----GGGGAG 624
                      |        ||||.||.|| ..||| |||||.|.|.|||    ...|||
455_051.nt.6     117 CC--------CGCGTCCCCA-TCGCC-GCGCCCGTCTGCTCCCCTCAGAG 156

Ovr107           625 GGCTTGCTGACGCTGCGGGCCAAGCCGCCCTCGGAGGCCGAGTACACCGA 674
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6     157 GGCTTGCTGACGCTGCGGGCCAAGCCGCCCTCGGAGGCCGAGTACACCGA 206

Ovr107           675 CGTGCTGCAGAAGATCAAGTACGCCTTCAGCCTGCTGGCCCGGCTGCGCG 724
                     ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6     207 CGTGCTGCAGAAGATCAAGTACGCCTTCAGCCTGCTGGCCCGGCTGCGCG 256
```

FIGURE 15 (continued)

```
Ovr107         725  GCAACATCGCCGACCCCTCCTCTCCGGAGCTGTTGCACTTCCTTTTCGGG  774
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6   257  GCAACATCGCCGACCCCTCCTCTCCGGAGCTGTTGCACTTCCTTTTCGGG  306

Ovr107         775  CCTCTGCAGATGATTGTGAACACGTCGGGGGGGCCGGAGTTCGCGAGCAG  824
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6   307  CCTCTGCAGATGATTGTGAACACGTCGGGGGGGCCGGAGTTCGCGAGCAG  356

Ovr107         825  TGTGCGGCGGCCGCATCTGACATCGGATGCCGTGGCGCTGCTGCGGGACA  874
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6   357  TGTGCGGCGGCCGCATCTGACATCGGATGCCGTGGCGCTGCTGCGGGACA  406

Ovr107         875  ACGTCACTCCACGTGAAAACGAGCTCTGGACCTCGCTGGGGGACTCGTGG  924
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6   407  ACGTCACTCCACGTGAAAACGAGCTCTGGACCTCGCTGGGGGACTCGTGG  456

Ovr107         925  ACCCGCCCCGGGCTGGAGCTGTCCCCGGAGGAGGGACCCCCATACAGACC  974
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6   457  ACCCGCCCCGGGCTGGAGCTGTCCCCGGAGGAGGGACCCCCATACAGACC  506

Ovr107         975  CGAGTTCTTCAGCGGCTGGGAGCCGCCGGTCACTGACCCGCAGAGCCGCG  024
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6   507  CGAGTTCTTCAGCGGCTGGGAGCCGCCGGTCACTGACCCGCAGAGCCGCG  556

Ovr107        1025  CCTGGGAGGACCCAGTTGAGAAACAGCTACAGCACGAGCGGAGGCGCCGG  074
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6   557  CCTGGGAGGACCCAGTTGAGAAACAGCTACAGCACGAGCGGAGGCGCCGG  606

Ovr107        1075  CAGCAAAGCGCCCCCCAGGTCGCTGTCAATGGTCACCGAGACTTGGAGCC  1124
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6   607  CAGCAAAGCGCCCCCCAGGTCGCTGTCAATGGTCACCGAGACTTGGAGCC  656

Ovr107        1125  AGAATCTGAGCCTCAGCTGGAGTCAGAGACAGCAGGAAAATGGGTCCTGT  1174
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6   657  AGAATCTGAGCCTCAGCTGGAGTCAGAGACAGCAGGAAAATGGGTCCTGT  706

Ovr107        1175  GTAATTATGACTTCCAGGCCCGCAACAGCAGTGAGCTGTCGGTCAAGCAG  1224
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6   707  GTAATTATGACTTCCAGGCCCGCAACAGCAGTGAGCTGTCGGTCAAGCAG  756

Ovr107        1225  CGGGACGTACTGGAGGTCCTGGATGACAGTCGTAAGTGGTGGAAGGTTCG  1274
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6   757  CGGGACGTACTGGAGGTCCTGGATGACAGTCGTAAGTGGTGGAAGGTTCG  806

Ovr107        1275  GGACCCAGCGGGGCAGGAGGGATATGTGCCCTACAACATCCTGACACCCT  1324
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6   807  GGACCCAGCGGGGCAGGAGGGATATGTGCCCTACAACATCCTGACACCCT  856

Ovr107        1325  ACCCCGGACCCCGGCTGCACCACAGCCAAAGCCCTGCCCGCAGCCTGAAC  1374
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6   857  ACCCCGGACCCCGGCTGCACCACAGCCAAAGCCCTGCCCGCAGCCTGAAC  906

Ovr107        1375  AGCACTCCTCCTCCACCACCAGCCCCAGCCCCGGCCCCACCTCCAGCTCT  1424
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6   907  AGCACTCCTCCTCCACCACCAGCCCCAGCCCCGGCCCCACCTCCAGCTCT  956

Ovr107        1425  GGCTCGGCCCCGCTGGGACAGGCCCCGCTGGGACAGCTGCGATAGCCTCA  1474
                    ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6   957  GGCTCGGCCCCGCTGGGACAGGCCCCGCTGGGACAGCTGCGATAGCCTCA  1006
```

FIGURE 15 (continued)

```
Ovr107        1475 ACGGCTTGGACCCCAGCGAGAAGGAGAAATTCTCCCAGATGCTCATCGTC 1524
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6  1007 ACGGCTTGGACCCCAGCGAGAAGGAGAAATTCTCCCAGATGCTCATCGTC 1056

Ovr107        1525 AACGAGGAACTGCAGGCGCGCCTGGCCCAGGGCCGCTCGGGACCGAGCCG 1574
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6  1057 AACGAGGAACTGCAGGCGCGCCTGGCCCAGGGCCGCTCGGGACCGAGCCG 1106

Ovr107        1575 CGCAGTCCCAGGGCCCCGCGCCCCGGAACCGCAGCTCAGCCCGGGCTCGG 1624
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6  1107 CGCAGTCCCAGGGCCCCGCGCCCCGGAACCGCAGCTCAGCCCGGGCTCGG 1156

Ovr107        1625 ACGCCTCCGAGGTCCGCGCCTGGCTGCAGGCCAAGGGCTTTAGCTCCGGG 1674
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6  1157 ACGCCTCCGAGGTCCGCGCCTGGCTGCAGGCCAAGGGCTTTAGCTCCGGG 1206

Ovr107        1675 ACCGTGGACGCGCTGGGTGTGCTGACCGGGGCGCAGCTTTTCTCGCTGCA 1724
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6  1207 ACCGTGGACGCGCTGGGTGTGCTGACCGGGGCGCAGCTTTTCTCGCTGCA 1256

Ovr107        1725 GAGGGAGGAGCTGCGGGCGGTGAGCCCCGAGGAGGGGGCACGTGTGTACA 1774
                   ||.|||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6  1257 GAAGGAGGAGCTGCGGGCGGTGAGCCCCGAGGAGGGGGCACGTGTGTACA 1306

Ovr107        1775 GCCAGGTCACCGTGCAGCGCTCGCTGCTGGAGGACAAAGAGAAAGTGTCA 1824
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6  1307 GCCAGGTCACCGTGCAGCGCTCGCTGCTGGAGGACAAAGAGAAAGTGTCA 1356

Ovr107        1825 GAGCTGGAGGCAGTGATGGAGAAGCAAAAGAAGAAGGTGGAAGGCGAGGT 1874
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6  1357 GAGCTGGAGGCAGTGATGGAGAAGCAAAAGAAGAAGGTGGAAGGCGAGGT 1406

Ovr107        1875 GGAAATGGAGGTCATTTGACCTGCCAGGCGCCCTTCGCAAAGAGTGACGA 1924
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6  1407 GGAAATGGAGGTCATTTGACCTGCCAGGCGCCCTTCGCAAAGAGTGACGA 1456

Ovr107        1925 GGCCCCGTGGGAGAACGGACTCCTCAGACTCTCCCCAATAGCGGAAGTCG 1974
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6  1457 GGCCCCGTGGGAGAACGGACTCCTCAGACTCTCCCCAATAGCGGAAGTCG 1506

Ovr107        1975 ATCTTCTGAAGGATGGCCAATCTGCTCCGGCCCTGGTCTTCCCCCATCCC 2024
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6  1507 ATCTTCTGAAGGATGGCCAATCTGCTCCGGCCCTGGTCTTCCCCCATCCC 1556

Ovr107        2025 GGTGGACAGACTTAACGATCCTTGCTGCAGTCCCTCCGGAGAGGATCTGG 2074
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6  1557 GGTGGACAGACTTAACGATCCTTGCTGCAGTCCCTCCGGAGAGGATCTGG 1606

Ovr107        2075 ACTGGCTGGGAGTGGGGAGGGCGTGGAGACAGTCTACGGAAAGCGCTAGC 2124
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6  1607 ACTGGCTGGGAGTGGGGAGGGCGTGGAGACAGTCTACGGAAAGCGCTAGC 1656

Ovr107        2125 AGACCCCCGAGAGGGTGCAGTGGAGCCCTGAGCATTGTAATATGCGGCCC 2174
                   ||||||||||||||||||||||||||||||||||||||||||||||||||
455_051.nt.6  1657 AGACCCCCGAGAGGGTGCAGTGGAGCCCTGAGCATTGTAATATGCGGCCC 1706

Ovr107        2175 AGCCTATAAACAGCCTCCGTGCTTAGCAAAAAAAAAAAAAAAAAAAA   2221
                   ||||||||||||||||||||||||||||.
455_051.nt.6  1707 AGCCTATAAACAGCCTCCGTGCTTAGCAG                      1735
```

FIGURE 16

```
Ovr110      1    GAGTCACCAAGGAAGGCAGCGGCAGCTCCACTCAGCCAGTACCCAGA   47
                   |||||||||||||||||||||||| ||||||||||||||||||||||
Ovr110v1    1  TGTGAGTCACCAAGGAAGGCAGCGGCA-CTCCACTCAGCCAGTACCCAGA   49

Ovr110     48  TACGCTGGGAACCTTCCCCAGCCATGGCTTCCCTGGGGCAGATCCTCTTC   97
               ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1   50  TACGCTGGGAACCTTCCCCAGCCATGGCTTCCCTGGGGCAGATCCTCTTC   99

Ovr110     98  TGGAGCATAATTAGCATCATCATTATTCTGGCTGGAGCAATTGCACTCAT  147
               ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1  100  TGGAGCATAATTAGCATCATCATTATTCTGGCTGGAGCAATTGCACTCAT  149

Ovr110    148  CATTGGCTTTGGTATTT---------------------------------  164
               |||||||||||||||||
Ovr110v1  150  CATTGGCTTTGGTATTTCAGAAGTCTCTGTCTGGCTTTCAGCAATGAAGG  199

Ovr110    165  --------------------------------------------------  164

Ovr110v1  200  GTTTGGTTGTAGAAGTTCCAAGGCTTCCCTTAGCATTGATCTTTGCTTCC  249

Ovr110    165  -------CAGGGAGACACTCCATCACAGTCACTACTGTCGCCTCAGCTGG  207
                      |||||||||||||||||||||||||||||||||||||||||||
Ovr110v1  250  TGAACTGCAGGGAGACACTCCATCACAGTCACTACTGTCGCCTCAGCTGG  299

Ovr110    208  GAACATTGGGGAGGATGGAATCCAGAGCTGCACTTTTGAACCTGACATCA  257
               ||||||||||||||||||||||.|||||||||||||||||||||||||||
Ovr110v1  300  GAACATTGGGGAGGATGGAATCCTGAGCTGCACTTTTGAACCTGACATCA  349

Ovr110    258  AACTTTCTGATATCGTGATACAATGGCTGAAGGAAGGTGTTTTAGGCTTG  307
               ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1  350  AACTTTCTGATATCGTGATACAATGGCTGAAGGAAGGTGTTTTAGGCTTG  399

Ovr110    308  GTCCATGAGTTCAAAGAAGGCAAAGATGAGCTGTCGGAGCAGGATGAAAT  357
               ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1  400  GTCCATGAGTTCAAAGAAGGCAAAGATGAGCTGTCGGAGCAGGATGAAAT  449

Ovr110    358  GTTCAGAGGCCGGACAGCAGTGTTTGCTGATCAAGTGATAGTTGGCAATG  407
               ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1  450  GTTCAGAGGCCGGACAGCAGTGTTTGCTGATCAAGTGATAGTTGGCAATG  499

Ovr110    408  CCTCTTTGCGGCTGAAAAACGTGCAACTCACAGATGCTGGCACCTACAAA  457
               ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1  500  CCTCTTTGCGGCTGAAAAACGTGCAACTCACAGATGCTGGCACCTACAAA  549

Ovr110    458  TGTTATATCATCACTTCTAAAGGCAAGGGGAATGCTAACCTTGAGTATAA  507
               ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1  550  TGTTATATCATCACTTCTAAAGGCAAGGGGAATGCTAACCTTGAGTATAA  599

Ovr110    508  AACTGGAGCCTTCAGCATGCCGGAAGTGAATGTGGACTATAATGCCAGCT  557
               ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1  600  AACTGGAGCCTTCAGCATGCCGGAAGTGAATGTGGACTATAATGCCAGCT  649

Ovr110    558  CAGAGACCTTGCGGTGTGAGGCTCCCCGATGGTTCCCCCAGCCCACAGTG  607
               ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1  650  CAGAGACCTTGCGGTGTGAGGCTCCCCGATGGTTCCCCCAGCCCACAGTG  699

Ovr110    608  GTCTGGGCATCCCAAGTTGACCAGGGAGCCAACTTCTCGGAAGTCTCCAA  657
               ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1  700  GTCTGGGCATCCCAAGTTGACCAGGGAGCCAACTTCTCGGAAGTCTCCAA  749
```

FIGURE 16 (continued)

```
Ovr110     658  TACCAGCTTTGAGCTGAACTCTGAGAATGTGACCATGAAGGTTGTGTCTG   707
                ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1   750  TACCAGCTTTGAGCTGAACTCTGAGAATGTGACCATGAAGGTTGTGTCTG   799

Ovr110     708  TGCTCTACAATGTTACGATCAACAACACATACTCCTGTATGATTGAAAAT   757
                ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1   800  TGCTCTACAATGTTACGATCAACAACACATACTCCTGTATGATTGAAAAT   849

Ovr110     758  GACATTGCCAAAGCAACAGGGGATATCAAAGTGACAGAATCGGAGATCAA   807
                ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1   850  GACATTGCCAAAGCAACAGGGGATATCAAAGTGACAGAATCGGAGATCAA   899

Ovr110     808  AAGGCGGAGTCACCTACAGCTGCTAAACTCAAAGGCTTCTCTGTGTGTCT   857
                ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1   900  AAGGCGGAGTCACCTACAGCTGCTAAACTCAAAGGCTTCTCTGTGTGTCT   949

Ovr110     858  CTTCTTTCTTTGCCATCAGCTGGGCACTTCTGCCTCTCAGCCCTTACCTG   907
                ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1   950  CTTCTTTCTTTGCCATCAGCTGGGCACTTCTGCCTCTCAGCCCTTACCTG   999

Ovr110     908  ATGCTAAAATAATGTGCCTCGGCCACAAAAAAGCATGCAAAGTCATTGTT   957
                |||||||||||||||||||.||||||||||||||||||||||||||||||
Ovr110v1  1000  TGCTAAAATAATGTGCCTTGGCCACAAAAAAGCATGCAAAGTCATTGTT   1049

Ovr110     958  ACAACAGGGATCTACAGAACTATTTCACCACCAGATATGACCTAGTTTTA   1007
                ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1  1050  ACAACAGGGATCTACAGAACTATTTCACCACCAGATATGACCTAGTTTTA   1099

Ovr110    1008  TATTTCTGGGAGGAAATGAATTCATATCTAGAAGTCTGGAGTGAGCAAAC   1057
                ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1  1100  TATTTCTGGGAGGAAATGAATTCATATCTAGAAGTCTGGAGTGAGCAAAC   1149

Ovr110    1058  AAGAGCAAGAAACAAAAAGAAGCCAAAAGCAGAAGGCTCCAATATGAACA   1107
                ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1  1150  AAGAGCAAGAAACAAAAAGAAGCCAAAAGCAGAAGGCTCCAATATGAACA   1199

Ovr110    1108  AGATAAATCTATCTTCAAAGACATATTAGAAGTTGGGAAAATAATTCATG   1157
                ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1  1200  AGATAAATCTATCTTCAAAGACATATTAGAAGTTGGGAAAATAATTCATG   1249

Ovr110    1158  TGAACTAGA-----------------------------------------   1166
                |||||||||
Ovr110v1  1250  TGAACTAGACAAGTGTGTTAAGAGTGATAAGTAAAATGCACGTGGAGACA   1299

Ovr110    1167  --------------------------------------------------   1166

Ovr110v1  1300  AGTGCATCCCCAGATCTCAGGGACCTCCCCCTGCCTGTCACCTGGGGAGT   1349

Ovr110    1167  --------------------------------------------------   1166

Ovr110v1  1350  GAGAGGACAGGATAGTGCATGTTCTTTGTCTCTGAATTTTTAGTTATATG   1399

Ovr110    1167  --------------------------------------------------   1166

Ovr110v1  1400  TGCTGTAATGTTGCTCTGAGGAAGCCCCTGGAAAGTCTATCCCAACATAT   1449

Ovr110    1167  --------------------------------------------------   1166

Ovr110v1  1450  CCACATCTTATATTCCACAAATTAAGCTGTAGTATGTACCCTAAGACGCT   1499
```

FIGURE 16 (continued)

```
Ovr110     1167 -------------------------------------------------- 1166

Ovr110v1   1500 GCTAATTGACTGCCACTTCGCAACTCAGGGGCGGCTGCATTTTAGTAATG 1549

Ovr110     1167 -------------------------------------------------- 1166

Ovr110v1   1550 GGTCAAATGATTCACTTTTTATGATGCTTCCAAAGGTGCCTTGGCTTCTC 1599

Ovr110     1167 -------------------------------------------------- 1166

Ovr110v1   1600 TTCCCAACTGACAAATGCCAAAGTTGAGAAAAATGATCATAATTTTAGCA 1649

Ovr110     1167 -------------------------------------------------- 1166

Ovr110v1   1650 TAAACAGAGCAGTCGGCGACACCGATTTTATAAATAAACTGAGCACCTTC 1699

Ovr110     1167 -------------------------------------------------- 1166

Ovr110v1   1700 TTTTTAAACAAACAAATGCGGGTTTATTTCTCAGATGATGTTCATCCGTG 1749

Ovr110     1167 -------------------------------------------------- 1166

Ovr110v1   1750 AATGGTCCAGGGAAGGACCTTTCACCTTGACTATATGGCATTATGTCATC 1799

Ovr110     1167 -------------------------------------------------- 1166

Ovr110v1   1800 ACAAGCTCTGAGGCTTCTCCTTTCCATCCTGCGTGGACAGCTAAGACCTC 1849

Ovr110     1167 -------------------------------------------------- 1166

Ovr110v1   1850 AGTTTTCAATAGCATCTAGAGCAGTGGGACTCAGCTGGGGTGATTTCGCC 1899

Ovr110     1167 -------------------------------------------------- 1166

Ovr110v1   1900 CCCCATCTCCGGGGGAATGTCTGAAGACAATTTTGGTTACCTCAATGAGG 1949

Ovr110     1167 -------------------------------------------------- 1166

Ovr110v1   1950 GAGTGGAGGAGGATACAGTGCTACTACCAACTAGTGGATAAAGGCCAGGG 1999

Ovr110     1167 -------------------------------------------------- 1166

Ovr110v1   2000 ATGCTGCTCAACCTCCTACCATGTACAGGACGTCTCCCCATTACAACTAC 2049

Ovr110     1167 ------------GTCAACTGTGTCAGGGCTAAGAAACCCTGGTTTTGAGT 1204
                            ||||||||||||||.|||||||||||||||||||||||
Ovr110v1   2050 CCAATCCGAAGTGTCAACTGTGTCAGGACTAAGAAACCCTGGTTTTGAGT 2099

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Ovr110     1305 CAGAGAGCCAGAACTCTATCGGGCACCAGGATAACATCTCTCAGTGAACA 1354
                ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1   2200 CAGAGAGCCAGAACTCTATCGGGCACCAGGATAACATCTCTCAGTGAACA 2249
```

FIGURE 16 (continued)

```
Ovr110     1355 GAGTTGACAAGGCCTATGGGAAATGCCTGATGGGATTATCTTCAGCTTGT  1404
                ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1   2250 GAGTTGACAAGGCCTATGGGAAATGCCTGATGGGATTATCTTCAGCTTGT  2299

Ovr110     1405 TGAGCTTCTAAGTTTCTTTCCCTTCATTCTACCCTGCAAGCCAAGTTCTG  1454
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Ovr110v1   2300 TGAGCTTCTAAGTTTCTTTCCCTTCATTCTACCCTGCAAGCCAAGTTCTG  2349

Ovr110     1455 TAAGAGAAATGCCTGAGTTCTAGCTCAGGTTTTCTTACTCTGAATTTAGA  1504
                ||||||||||||||||||||||||||||||||||||||||||||||||||
Ovr110v1   2350 TAAGAGAAATGCCTGAGTTCTAGCTCAGGTTTTCTTACTCTGAATTTAGA  2399

Ovr110     1505 TCTCCAGACCCTGCCTGGCCACAATTCAAATTAAGGCAACAAACATATAC  1554
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Ovr110v1   2400 TCTCCAGACCCTTCCTGGCCACAATTCAAATTAAGGCAACAAACATATAC  2449

Ovr110     1555 CTTCCATGAAGCACACACAGACTTTTGAAAGCAAGGACAATGACTGCTTG  1604
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Ovr110     1605 AATTGAGGCCTTGAGGAATGAAGCTTTGAAGGAAAAGAATACTTTGTTTC  1654
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Ovr110v1   2500 AATTGAGGCCTTGAGGAATGAAGCTTTGAAGGAAAAGAATACTTTGTTTC  2549

Ovr110     1655 CAGCCCCCTTCCCACACTCTTCATGTGTTAACCACTGCCTTCCTGGACCT  1704
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                ||||||||||||||||||||||||||||||||||||||||||||||||||
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Ovr110     1755 GTTCTGATCGTTCAAGAGAATGATTAAATATACATTTCCTAAAAAAAAAA  1804
                |||||||||||||||||||||||||||||||||||||||||
Ovr110v1   2650 GTTCTGATCGTTCAAGAGAATGATTAAATATACATTTCCTA           2690

Ovr110     1805 AAAAAAA                                             1811

Ovr110v1   2691                                                     2690
```

FIGURE 17

```
Ovr110          1 MASLGQIILFWSIISIIIILAGAIALIIGFGISGRHSITVTTVASAGNIGE   50
                  ||||||||||||||||||||||||||||||||   .::|...|..|.:.|
455_053.aa.2    1 MASLGQIILFWSIISIIIILAGAIALIIGFGIS---EVSVWLSAMKGLVVE   47

Ovr110         51 DGIQSCTFEPDIKLSDIVIQWLKEGVLGLVHEFKEGKDELSEQDEMFRGR  100
                          .|.:.|:.|...
455_053.aa.2   48 --------VPRLPLALIFAS                                  59

Ovr110        101 TAVFADQVIVGNASLRLKNVQLTDAGTYKCYIITSKGKGNANLEYKTGAF  150

455_053.aa.2   60                                                    59

Ovr110        151 SMPEVNVDYNASSETLRCEAPRWFPQPTVVWASQVDQGANFSEVSNTSFE  200

455_053.aa.2   60                                                    59

Ovr110        201 LNSENVTMKVVSVLYNVTINNTYSCMIENDIAKATGDIKVTESEIKRRSH  250

455_053.aa.2   60                                                    59

Ovr110        251 LQLLNSKASLCVSSFFAISWALLPLSPYLMLK                    282

455_053.aa.2   60                                                    59
```

FIGURE 18

```
Ovr110          1 MASLGQILFWSIISIIIILAGAIALIIGFGISGRHSITVTTVASAGNIGE    50
                                                     .:|||||||||||||||||||
455_053.aa.3    1                                    TAGRHSITVTTVASAGNIGE    20

Ovr110         51 DGIQSCTFEPDIKLSDIVIQWLKEGVLGLVHEFKEGKDELSEQDEMFRGR   100
                  |||.||||||||||||||||||||||||||||||||||||||||||||||
455_053.aa.3   21 DGILSCTFEPDIKLSDIVIQWLKEGVLGLVHEFKEGKDELSEQDEMFRGR    70

Ovr110        101 TAVFADQVIVGNASLRLKNVQLTDAGTYKCYIITSKGKGNANLEYKTGAF   150
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_053.aa.3   71 TAVFADQVIVGNASLRLKNVQLTDAGTYKCYIITSKGKGNANLEYKTGAF   120

Ovr110        151 SMPEVNVDYNASSETLRCEAPRWFPQPTVVWASQVDQGANFSEVSNTSFE   200
                  ||||||||||||||||||||||||||||||||||||||||||||||||||
455_053.aa.3  121 SMPEVNVDYNASSETLRCEAPRWFPQPTVVWASQVDQGANFSEVSNTSFE   170

Ovr110        201 LNSENVTMKVVSVLYNVTINNTYSCMIENDIAKATGDIKVTESEIKRRSH   250
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455_053.aa.3  171 LNSENVTMKVVSVLYNVTINNTYSCMIENDIAKATGDIKVTESEIKRRSH   220

Ovr110        251 LQLLNSKASLCVSSFFAISWALLPLSPYLMLK                     282
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Turner, Leah
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aagtgttggg acagaaagta ctttatgtaa ctaagtgggc tgttcagaag cttagaggtc 540

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agaaagcctt tatttacttt gtggaaattg aacaagaaat gcatctgtct tagaaactgg 660

agattattga tgttaggtaa cacatgtaat ggttctcgtg gcaattgtgt ctcagtattt 720

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gttcagccgc gctgccgaga agctttacct cgctgaccct atgaaggcac gtgtggttct 240

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<213> Homo sapien

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<211> 924
<212> DNA

<213> Homo sapien

<400> 85
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<211> 847
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<213> Homo sapien

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<211> 3429
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<213> Homo sapien

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<213> Homo sapien

<400> 89
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tacaaagaaa tgg 1633

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<212> DNA
<213> Homo sapien

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gctttgaaat tagcacttat ttctgtactg ttgtgtccca ccctcctcaa aaggacacgt 1740
tcaagtggct tccagtgtta aaatggtgag tgatgtgatg ttgaaatgtt tcacctgagt 1800
tctgagcttt tccatccgta taatcatagg tacga 1835

<210> 129
<211> 438
<212> PRT
<213> Homo sapien

<400> 129

Pro Val Pro Ala Leu Cys Pro Ser Pro Trp Pro Cys Pro Pro Ala Cys
1 5 10 15

Pro Ala Pro Ser Gly Pro Pro Ser Leu Asn Ser Ile Pro Leu Ala Leu
20 25 30

Phe His Ser Glu Glu Pro His Gly Cys Phe Ser Leu Ala Glu Arg Pro
35 40 45

Ser Pro Pro Lys Ala Trp Asp Gln Leu Arg Ala Val Ser Gly Gly Ser
50 55 60

Pro Glu Arg Arg Thr Pro Trp Lys Pro Pro Pro Ser Asp Leu Tyr Gly
65 70 75 80

Asp Leu Lys Ser Arg Arg Asn Ser Val Ala Ser Pro Thr Ser Pro Thr
85 90 95

Arg Ser Leu Pro Arg Ser Ala Ser Ser Phe Glu Gly Arg Ser Val Pro
100 105 110

Ala Thr Pro Val Leu Thr Arg Gly Ala Gly Pro Gln Leu Cys Lys Pro
115 120 125

Glu Gly Leu His Ser Arg Gln Trp Ser Gly Ser Gln Asp Ser Gln Met
130 135 140

Gly Phe Pro Arg Ala Asp Pro Ala Ser Asp Arg Ala Ser Leu Phe Val
145 150 155 160

Ala Arg Thr Arg Arg Ser Asn Ser Ser Glu Ala Leu Leu Val Asp Arg
165 170 175

Ala Ala Gly Gly Gly Ala Gly Ser Pro Pro Ala Pro Leu Ala Pro Ser
180 185 190

Ala Ser Gly Pro Pro Val Cys Lys Ser Ser Glu Val Leu Tyr Glu Arg
195 200 205

Pro Gln Pro Thr Pro Ala Phe Ser Ser Arg Thr Ala Gly Pro Pro Asp

210 215 220

Pro Pro Arg Ala Ala Arg Pro Ser Ser Ala Ala Pro Ala Ser Arg Gly
225 230 235 240

Ala Pro Arg Leu Pro Pro Val Cys Gly Asp Phe Leu Leu Asp Tyr Ser
245 250 255

Leu Asp Arg Gly Leu Pro Arg Ser Gly Gly Gly Thr Gly Trp Gly Glu
260 265 270

Leu Pro Pro Ala Ala Glu Val Pro Gly Pro Leu Ser Arg Arg Asp Gly
275 280 285

Leu Leu Thr Met Leu Pro Gly Pro Pro Pro Val Tyr Ala Ala Asp Ser
290 295 300

Asn Ser Pro Leu Leu Arg Thr Lys Asp Pro His Thr Arg Ala Thr Arg
305 310 315 320

Thr Lys Pro Cys Gly Leu Pro Pro Glu Ala Ala Glu Gly Pro Glu Val
325 330 335

His Pro Asn Pro Leu Leu Trp Met Pro Pro Pro Thr Arg Ile Pro Ser
340 345 350

Ala Gly Glu Arg Ser Gly His Lys Asn Leu Ala Leu Glu Gly Leu Arg
355 360 365

Asp Trp Tyr Ile Arg Asn Ser Gly Leu Ala Ala Gly Pro Gln Arg Arg
370 375 380

Pro Val Leu Pro Ser Val Gly Pro Pro His Pro Pro Phe Leu His Ala
385 390 395 400

Arg Cys Tyr Glu Val Gly Gln Ala Leu Tyr Gly Ala Pro Ser Gln Ala
405 410 415

Pro Leu Pro His Ser Arg Ser Phe Thr Ala Pro Pro Val Ser Gly Arg
420 425 430

Tyr Gly Gly Cys Phe Tyr
435

<210> 130
<211> 237

<212> PRT
<213> Homo sapien

<400> 130

Met Glu Val Lys Gly Gln Leu Ile Ser Ser Pro Thr Phe Asn Ala Pro
1 5 10 15

Ala Ala Leu Phe Gly Glu Ala Ala Pro Gln Val Lys Ser Glu Arg Leu
20 25 30

Arg Gly Leu Leu Asp Arg Gln Arg Thr Leu Gln Glu Ala Leu Ser Leu
35 40 45

Lys Leu Gln Glu Leu Arg Lys Val Cys Leu Gln Glu Ala Glu Leu Thr
50 55 60

Gly Gln Leu Pro Pro Glu Cys Pro Leu Glu Pro Gly Glu Arg Pro Gln
65 70 75 80

Leu Val Arg Arg Arg Pro Pro Thr Ala Arg Ala Tyr Pro Pro Pro His
85 90 95

Pro Asn Gln Ala His His Ser Leu Cys Pro Ala Glu Glu Leu Ala Leu
100 105 110

Glu Ala Leu Glu Arg Glu Val Ser Val Gln Gln Gln Ile Ala Ala Ala
115 120 125

Ala Arg Arg Leu Ala Leu Ala Pro Asp Leu Ser Thr Glu Gln Arg Arg
130 135 140

Arg Arg Arg Gln Val Gln Ala Asp Ala Leu Arg Arg Leu His Glu Leu
145 150 155 160

Glu Glu Gln Leu Arg Asp Val Arg Ala Arg Leu Gly Leu Pro Val Leu
165 170 175

Pro Leu Pro Gln Pro Leu Pro Leu Ser Thr Gly Ser Val Ile Thr Thr
180 185 190

Gln Gly Val Cys Leu Gly Met Arg Leu Ala Gln Leu Ser Gln Gly Glu
195 200 205

His Pro Leu Val Arg Val Gly Glu Trp Thr Leu Ala Asn Gly Arg Gly
210 215 220

Arg Ala Gly Met Gly Asp Trp Pro Val Lys Thr Gly Arg
225 230 235

<210> 131
<211> 233
<212> PRT
<213> Homo sapien

<400> 131

Met Pro Phe Gln Lys Gly Met Pro Phe Asp Leu Cys Phe Leu Val Gln
1 5 10 15

Ser Ser Asp Phe Lys Val Met Val Asn Gly Ile Leu Phe Val Gln Tyr
20 25 30

Phe His Arg Val Pro Phe His Arg Val Asp Thr Ile Ser Val Asn Gly
35 40 45

Ser Val Gln Leu Ser Tyr Ile Ser Phe Gln Pro Pro Gly Val Trp Pro
50 55 60

Ala Asn Pro Ala Pro Ile Thr Gln Thr Val Ile His Thr Val Gln Ser
65 70 75 80

Ala Pro Gly Gln Met Phe Ser Thr Pro Ala Ile Pro Pro Met Met Tyr
85 90 95

Pro His Pro Ala Tyr Pro Met Pro Phe Ile Thr Thr Ile Leu Gly Gly
100 105 110

Leu Tyr Pro Ser Lys Ser Ile Leu Leu Ser Gly Thr Val Leu Pro Ser
115 120 125

Ala Gln Arg Phe His Ile Asn Leu Cys Ser Gly Asn His Ile Ala Phe
130 135 140

His Leu Asn Pro Arg Phe Asp Glu Asn Ala Val Val Arg Asn Thr Gln
145 150 155 160

Ile Asp Asn Ser Trp Gly Ser Glu Glu Arg Ser Leu Pro Arg Lys Met
165 170 175

Pro Phe Val Arg Gly Gln Ser Phe Ser Val Trp Ile Leu Cys Glu Ala
180 185 190

His Cys Leu Lys Val Ala Val Asp Gly Gln His Leu Phe Glu Tyr Tyr
195 200 205

His Arg Leu Arg Asn Leu Pro Thr Ile Asn Arg Leu Glu Val Gly Gly
210 215 220

Asp Ile Gln Leu Thr His Val Gln Thr
225 230

<210> 132
<211> 115
<212> PRT
<213> Homo sapien

<400> 132

Met Glu Lys Ser Gly Arg Arg Trp Leu Ala Ser Ala Ala Pro Pro Leu
1 5 10 15

Gly Arg Leu Arg Arg Arg Glu Ser Gly Ala Glu Gln Gly Gly Leu Ser
20 25 30

Val Arg Ala Thr Arg Val Ser Leu Val Arg Ser Ala Leu Asp Cys Ala
35 40 45

Pro Arg Ser Gly Val Arg Arg Pro Gly Ser Cys Phe Cys Arg Cys Arg
50 55 60

Arg Arg Ile Pro Val Ala Arg Arg Ala Arg Leu Pro Gln Ala Cys Ser
65 70 75 80

Gln His Arg Thr Glu Pro Ser Gly Gly Arg Gly Trp Ser Ala Arg Pro
85 90 95

Ala Trp Glu Arg Gln Gly Arg Arg Cys Asn Leu Leu Thr Ala Lys Lys
100 105 110

Pro Gly Glu
115

<210> 133
<211> 151
<212> PRT
<213> Homo sapien

<400> 133

Arg Asn Glu Tyr Gln Leu Met Leu Thr Arg Tyr Leu Asp Phe Glu Gly
1 5 10 15

Leu Pro Ser Lys Leu Trp His Glu Ser Val Arg His Gly Phe Leu His

20 25 30

Ser Ser Asp Asn Leu Phe Phe Gln Asn Gly Phe Leu Leu Leu Leu Leu
35 40 45

Leu Thr Asn Ser Lys His Pro Val Leu Leu Phe Val Leu Phe Val Leu
50 55 60

Phe Cys Phe Val Leu Phe Cys Leu Pro Phe Arg Lys Val Leu Phe Arg
65 70 75 80

Val Gly Ile Asp Cys Ser Leu Glu Thr Leu Ser Ser Val Cys Ala Gly
85 90 95

Ser Val His Ala Leu Tyr Glu Phe Gly Leu Asn Asn Ala Phe Glu Val
100 105 110

Thr Trp Asp Val Gln Phe Trp His Val Phe Ile Asp Cys Val Phe Lys
115 120 125

His Val Ser Cys Phe Met Ser Phe Ser Lys Pro His Phe Thr Ser Tyr
130 135 140

Ser Glu Lys Leu Ile Lys Glu
145 150

<210> 134
<211> 699
<212> PRT
<213> Homo sapien

<400> 134

Met Arg His Ser Ile Ser Asn Leu Lys Lys Lys Lys Lys Lys Lys Lys
1 5 10 15

Lys Thr Ser Gly Lys Lys Val Arg Gly Ile Leu Ser Leu Lys Leu Val
20 25 30

Ser Glu Gly Thr Gly Glu Glu Lys Thr Thr Val Pro Asn Glu Lys Arg
35 40 45

Thr Gly Asn Leu Ile Leu Ile Gly Met His Gln Ile Leu Leu Cys Thr
50 55 60

Phe Ala Ser Ser Ile Ser Arg Arg Ile Val Gln Asn Val Tyr Phe Leu
65 70 75 80

Pro Met Leu Arg Lys Gln Val Tyr Arg Thr Tyr Ser Gly Leu Ile Ala
85 90 95

Ser Glu Trp Gln Ile Arg Ile Gly Ile Gln Ser Pro Cys Cys Gly Leu
100 105 110

Leu Gln Gln Glu Asn Gln Ala Thr Gln Met Ile Leu Phe Ser Leu Phe
115 120 125

Gly Phe Val Lys Cys His Leu Val Leu Phe Pro Ser Asn Ile Glu Glu
130 135 140

Val Val Gly Leu Lys Leu Trp Asp Leu His Tyr Ala Tyr Thr Phe Leu
145 150 155 160

Phe Met Pro Leu Phe Arg Glu Ala Asp Tyr Cys Phe Phe Lys Met Met
165 170 175

His Trp Arg Arg Cys Glu Ser Lys Ile Ala Thr Trp His Tyr Leu Pro
180 185 190

Arg Ile Asn Glu Lys Gly Lys Lys Thr Ile Phe Ser Phe Phe Lys His
195 200 205

Phe Ser Glu Lys Ile Gln Leu Pro Phe Leu Ile Gly Glu Arg His His
210 215 220

Ala Arg Leu Ile Phe Ala Phe Leu Val Glu Thr Gly Phe His His Val
225 230 235 240

Gly Gln Asp Gly Leu Asp Leu Leu Ile Ser Cys Ser Ala His Leu Gly
245 250 255

Leu Leu Ser Ala Gly Ile Thr Gly Met Ser His Cys Ala Arg Ser Thr
260 265 270

Ile Leu Phe Ser Val Ser His Pro Tyr Gln Ile Ile Glu Pro Ser Val
275 280 285

Cys Met Phe Leu Asn Leu Val Tyr Asn Ser Thr Ser Leu Thr Tyr Lys
290 295 300

Ser Thr Ile Ser Tyr Glu Phe Phe Ile Glu Val Gly Ser Ile Leu Lys
305 310 315 320

Trp Thr Glu Asn Leu Ile Pro Gly Arg Ala Arg Trp Leu Met Pro Val
325 330 335

Ile Pro Tyr Phe Gly Arg Pro Arg Trp Val Asp His Leu Arg Leu Gly
340 345 350

Val Arg Asp Gln Pro Gly Gln His Gly Glu Thr Pro Ser Leu Leu Lys
355 360 365

Asn Thr Lys Ile Ser Gln Ala Trp Trp Leu Ser Val Ile Pro Ala Asn
370 375 380

Gly Glu Ala Glu Ala Gln Glu Ser Leu Glu Pro Glu Glu Ala Glu Val
385 390 395 400

Ala Val Ser Arg Asp His Thr Thr Ala Leu His Pro Gly Gln Trp Ser
405 410 415

Glu Thr Leu Ser Gln Lys Ile Ile Asn Glu Asp Met Ile Pro Ala Cys
420 425 430

Phe Ile Gln Leu Glu Arg His Thr Thr His Glu Ile Ile Gly Glu His
435 440 445

Val Asn Val Tyr Leu Leu Val Gln Leu Arg Lys Arg Glu Glu Tyr Val
450 455 460

Leu Val Ser Lys Val Leu Asn Lys Thr Glu Val Ala Ser Thr Val Ala
465 470 475 480

His Val Phe Phe Gly Leu Thr Phe Phe Phe Ser Ser Thr Phe Cys Asn
485 490 495

Phe Tyr Asp Leu Gly His Glu Val Leu Pro Leu Arg His Asn Gln Tyr
500 505 510

Pro Ser Arg Lys Gly Leu Leu Ile Pro Gly Val Lys Ile Pro Ser Leu
515 520 525

Arg Gly Ser His Tyr Gly Ser Pro Gly Val Lys Ile Pro Ser Ser Gln
530 535 540

Glu Ser Tyr Leu Gln His Leu Gly Lys Ile Pro Glu Gly Ala Thr Ser
545 550 555 560

Asn Arg Lys Met Lys Glu Arg Phe Asn Phe Ser Thr Gln Val Thr Asn

565 570 575

Pro Met His Ser Ile Val Tyr Val Ile Cys Arg Lys Gly Thr Gly Gly
580 585 590

Val Arg Ala Leu Trp Val Thr Ala Leu Leu Val Val Thr Phe Thr Leu
595 600 605

Leu Phe Leu Leu Asn Leu Trp Phe Ser Arg Leu Lys Asn Glu Ile Ile
610 615 620

Gly Gln Ile Asn Ser Ser Gln Pro Phe Leu Glu Gln Gln Ile Arg Leu
625 630 635 640

Ser Leu Lys Ser Phe Ser Lys Ile Ser Cys Phe Gln Ser Leu Pro Val
645 650 655

Ile Ala Ile Ile Pro Arg Leu Ile Lys Ser Val Leu Val Asn Gln Phe
660 665 670

Leu Tyr Phe Phe Phe Leu Ser Phe Phe Tyr Ser Val Phe Arg Tyr His
675 680 685

Leu Thr Asn Asn Leu Leu Leu Ile Leu Leu Arg
690 695

<210> 135
<211> 151
<212> PRT
<213> Homo sapien

<400> 135

Arg Asn Glu Tyr Gln Leu Met Leu Thr Arg Tyr Leu Asp Phe Glu Gly
1 5 10 15

Leu Pro Ser Lys Leu Trp His Glu Ser Val Arg His Gly Phe Leu His
20 25 30

Ser Ser Asp Asn Leu Phe Phe Gln Asn Gly Phe Leu Leu Leu Leu Leu
35 40 45

Leu Thr Asn Ser Lys His Pro Val Leu Leu Phe Val Leu Phe Val Leu
50 55 60

Phe Cys Phe Val Leu Phe Cys Leu Pro Phe Arg Lys Val Leu Phe Arg
65 70 75 80

Val Gly Ile Asp Cys Ser Leu Glu Thr Leu Ser Ser Val Cys Ala Gly
85 90 95

Ser Val His Ala Leu Tyr Glu Phe Gly Leu Asn Asn Ala Phe Glu Val
100 105 110

Thr Trp Asp Val Gln Phe Trp His Val Phe Ile Asp Cys Val Phe Lys
115 120 125

His Val Ser Cys Phe Met Ser Phe Ser Lys Pro His Phe Thr Ser Tyr
130 135 140

Ser Glu Lys Leu Ile Lys Glu
145 150

<210> 136
<211> 762
<212> PRT
<213> Homo sapien

<400> 136

Met Gly Arg Leu Arg His Lys Asn Leu Leu Asn Leu Gly Gly Gly Gly
1 5 10 15

Cys Ser Glu Pro Arg Ser His His Cys Thr Pro Ser Trp Ala Met Glu
20 25 30

Arg Asp Ser Val Ser Lys Asn Asn Lys Glu Asp Met Ile Pro Ala Cys
35 40 45

Phe Ile Gln Leu Glu Arg His Thr Thr His Glu Ile Ile Gly Glu His
50 55 60

Val Asn Val Tyr Leu Leu Val Gln Leu Arg Lys Arg Glu Glu Tyr Val
65 70 75 80

Leu Val Ser Lys Val Leu Asn Lys Thr Glu Val Ala Ser Thr Val Ala
85 90 95

His Val Phe Phe Gly Leu Thr Phe Phe Phe Ser Ser Thr Phe Cys Asn
100 105 110

Phe Tyr Asp Leu Gly His Glu Val Leu Pro Leu Arg His Asn Gln Tyr
115 120 125

Pro Ser Arg Lys Gly Leu Leu Ile Pro Gly Val Lys Ile Pro Ser Leu

130 135 140

Arg Gly Ser His Tyr Val Ile Pro Arg Ser Lys Asp Ser Tyr Leu Ala
145 150 155 160

Gly Ile Leu Leu Ala His Leu Gly Lys Ile Pro Glu Gly Ala Thr Ser
165 170 175

Asn Arg Lys Met Lys Glu Arg Phe Asn Phe Ser Thr Gln Val Thr Asn
180 185 190

Pro Met His Ser Ile Val Tyr Val Ile Cys Arg Lys Gly Thr Gly Gly
195 200 205

Val Arg Ala Leu Trp Val Thr Ala Leu Leu Val Val Thr Phe Thr Leu
210 215 220

Leu Phe Leu Leu Asn Leu Trp Phe Ser Arg Leu Lys Asn Glu Ile Ile
225 230 235 240

Gly Gln Ile Asn Ser Ser Gln Pro Phe Leu Glu Gln Gln Ile Arg Leu
245 250 255

Ser Leu Lys Ser Phe Ser Lys Ile Ser Cys Phe Gln Ser Leu Pro Val
260 265 270

Ile Ala Ile Ile Pro Arg Leu Ile Lys Ser Val Leu Val Asn Gln Phe
275 280 285

Leu Tyr Phe Phe Phe Leu Ser Phe Phe Tyr Ser Val Phe Gln Val Ser
290 295 300

Phe Asp Gln Gln Leu Ala Leu Asn Leu Thr Ala Met Thr Glu Ile Ser
305 310 315 320

Lys Glu Glu Ser Ile Val Val Ile Gly Leu Val Ile Ile Ile Leu Lys
325 330 335

Thr Ile His Tyr Phe Leu Lys Leu Asn Ala Val Cys Leu Ile Ser Val
340 345 350

Glu Tyr Asp Lys Asn Val Asn Glu Lys Pro Asn Met Thr Leu Thr Leu
355 360 365

Ala Leu Asn Phe Ile Phe Thr Cys Val Leu Lys Val Leu Tyr Trp Pro
370 375 380

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Val Gly Lys Leu Ile Cys Ile Arg Phe Thr Pro Gly Phe Gly Arg Asn
385                 390                 395                 400

Ser Phe Leu Lys Ile Gln Leu Ala Asp Leu Lys Met Phe Phe Ile Pro
                405                 410                 415

Gln Asn Val Ser Leu Leu Cys His Ser Tyr Arg Leu Ser Ala Phe Phe
            420                 425                 430

Asp His His Val Asn Tyr Ala Val Val Asn His Gly Val Gln Ala Asp
        435                 440                 445

Glu Leu Val Val Phe Val Lys Gln Asn Val Met Ser Ile Gly Arg Asp
    450                 455                 460

Ser Ser Ser Gly Glu His Gly Ser Phe Pro Val Ile Pro Ala Leu Met
465                 470                 475                 480

Asn Arg Leu Lys Thr Ala Val Tyr Tyr Gly Gln Phe Asn Phe Thr Gly
                485                 490                 495

Leu Pro Gly Leu Ala Phe Gln Leu Leu Ser Cys Arg Glu Thr Trp Cys
            500                 505                 510

Cys Thr Val His Ile Leu Glu Lys Trp Gln Glu Cys Ser Leu Glu Leu
        515                 520                 525

Gln Ile Thr Gln Gln Arg Ile Pro Tyr Gln Tyr Ile Gly Phe Ser Cys
    530                 535                 540

Tyr Ile Glu Ile Trp Tyr Phe Ser Asp Gly Tyr Gly Phe Cys Leu Thr
545                 550                 555                 560

Cys Val Ser Val Leu Leu Glu Arg Gln Tyr Arg Ile Lys Asn Phe Leu
                565                 570                 575

Met Ser Phe Leu Lys Ile Glu Ile Ile Met Ala Leu Leu Val Val Leu
            580                 585                 590

Cys Ser Asp Arg Pro Leu Ile Lys Lys Ser Phe Asn Pro Ala Phe His
        595                 600                 605

Phe Thr Ser Pro Pro Phe Ile Phe Asn Ile His Ser Leu Lys Ile Val
    610                 615                 620
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Met Ile Phe Ser Val Ile Gly Tyr Val Lys Lys Phe His Phe Lys Val
625 630 635 640

Leu Ile Cys Asn Asn Leu His Phe Leu Leu Asn Trp Arg Thr Phe Leu
645 650 655

Arg Gln Thr Tyr Phe Tyr Glu Leu Ile Phe Ser Leu Val Lys Glu Asn
660 665 670

Ser Leu Val Ser Tyr Arg Glu Trp Leu Ala Leu Cys Ile Pro His Pro
675 680 685

Leu Cys Gly Leu Pro Val Ala Val Val Leu Leu Lys Ile Ala Asp Ile
690 695 700

Leu Ile Asn Met Met Ile Phe Gly Thr Gly Leu Ser Leu Leu Leu Ile
705 710 715 720

Ser Asn Lys Val Gly Gln Ser Asn Leu Asn Tyr Phe Asn Lys His Asn
725 730 735

Leu Ala Phe Leu Tyr Met Arg Lys Tyr Phe Gln Lys Ile Thr Arg Phe
740 745 750

Ile Ser Arg Ile Arg Asp Gly Lys Tyr Gln
755 760

<210> 137
<211> 138
<212> PRT
<213> Homo sapien

<400> 137

Met Leu Ala Asn Asp Val Arg His Gln Gln Glu Met Trp Gly Phe Arg
1 5 10 15

Lys Val Glu Gly Gly Val Val Gln Ser Leu Gly Lys Ser Ser Val Glu
20 25 30

Gly Glu Thr Asp Gly Thr Ile Ser Glu Phe Arg Glu Ile Gln Arg Leu
35 40 45

Ala Ala Phe Ala Ser Phe Leu Ser His Ala Pro Pro Leu Asn Ala Arg
50 55 60

Arg Leu Leu Thr Pro Pro Pro Arg Arg Arg Pro Arg Cys Thr Pro Ala

65 70 75 80

Ala Ala Met Ala Asp Val Ser Glu Arg Thr Leu Gln Leu Ser Val Leu
85 90 95

Val Ala Phe Ala Ser Gly Val Leu Leu Gly Trp Gln Ala Asn Arg Leu
100 105 110

Arg Arg Arg Tyr Leu Asp Trp Arg Lys Arg Arg Leu Gln Asp Lys Leu
115 120 125

Ala Ala Thr Gln Lys Lys Leu Asp Leu Ala
130 135

<210> 138
<211> 179
<212> PRT
<213> Homo sapien

<400> 138

Met Pro Cys Ala Arg Ala Gly Gly Leu Gly Leu Gln Thr Pro Asn Leu
1 5 10 15

Asn Gly His Pro Arg Ala Glu Pro Pro Glu Gly Thr Gly Gly Phe His
20 25 30

Phe Gln Thr Gly Ile Leu Ala Ala Ser Leu Leu Pro Pro Ala Glu Glu
35 40 45

Glu Thr Leu Leu Tyr Ile Leu Thr Phe Cys Arg Gln Val Lys Arg Arg
50 55 60

Thr Gln Thr Phe Gly Asp Glu Arg Glu Thr Lys Thr Glu Pro Ser Val
65 70 75 80

Gln Val Thr Ala Ser Gln Ser Arg His Leu Thr Asp Pro Thr Tyr Cys
85 90 95

Leu Phe Leu Asn Met Asn Asp Cys Arg Ser Leu Pro Glu Thr Val Ser
100 105 110

Glu Lys Thr Ala Thr Ser Tyr Phe Leu Tyr Val Phe Pro Ile Lys Arg
115 120 125

Leu Ser Trp Val Gly Leu Arg Ile Thr Glu Gly Lys Arg Ser Gln Phe
130 135 140

Gln Val Thr Gln Ala Ile Phe Cys Val Lys Arg Glu Gln Asp Lys Ser
145 150 155 160

Gln Pro Gln Gln Gln Asn Pro Lys Pro Pro Leu Arg Leu Leu Trp Gln
165 170 175

Ser Asn Thr

<210> 139
<211> 294
<212> PRT
<213> Homo sapien

<400> 139

Ile Ser Val Leu Thr Trp Ala Val Phe Thr Pro Pro Leu Pro Ser Arg
1 5 10 15

Tyr Phe Ser Cys Ala His Ser Thr Asp Arg Glu Ala Glu Ala Gly Glu
20 25 30

Val Arg Thr Arg Leu Arg Ser Tyr Gly Leu Pro Trp Asp Leu Ala Glu
35 40 45

Asp Gly Gly Arg Ala Gly Pro Ser Gly Leu Glu Thr Leu Thr Pro Tyr
50 55 60

Ser Pro Thr Pro Ser Phe Thr Trp Ser Asp Ala Arg Leu His Arg Gly
65 70 75 80

Leu Val Thr Leu Leu Thr Gly Glu Ile Val Asp Ala Phe Ser Leu Glu
85 90 95

Phe Arg Thr Leu Tyr Ala Ala Ser Cys Pro Leu Pro Pro Ala Pro Pro
100 105 110

Gln Lys Pro Ser Val Ile Gly Gly Leu Gln Arg Gly Arg Ser Leu His
115 120 125

Arg Val Ser Arg Arg Arg Ser Val Ala Pro Ala Ser Pro Pro Pro Pro
130 135 140

Asp Gly Pro Leu Ala His Arg Leu Ala Ala Cys Arg Val Ser Pro Ala
145 150 155 160

Thr Pro Gly Pro Ala Leu Ser Asp Ile Leu Arg Ser Val Gln Arg Ala

165 170 175

Arg Thr Pro Ser Gly Pro Pro Ala Arg Pro Ser Arg Ser Met Trp Asp
180 185 190

Leu Ser Arg Leu Ser Gln Leu Ser Gly Ser Ser Asp Gly Asp Asn Glu
195 200 205

Leu Lys Lys Ser Trp Gly Ser Lys Asp Thr Pro Ala Lys Ala Leu Met
210 215 220

Arg Gln Arg Gly Thr Gly Gly Gly Pro Trp Gly Glu Val Asp Ser Arg
225 230 235 240

Pro Pro Trp Gly Gly Ala Leu Pro Leu Pro Pro Ala His Arg Leu Arg
245 250 255

Tyr Leu Ser Pro Ala Arg Arg Arg Phe Gly Gly Asp Ala Thr Phe Lys
260 265 270

Leu Gln Glu Pro Arg Gly Val Arg Pro Ser Asp Trp Ala Pro Arg Ala
275 280 285

Gly Leu Gly Gly Gln Pro
290

<210> 140
<211> 294
<212> PRT
<213> Homo sapien

<400> 140

Ile Ser Val Leu Thr Trp Ala Val Phe Thr Pro Pro Leu Pro Ser Arg
1 5 10 15

Tyr Phe Ser Cys Ala His Ser Thr Asp Arg Glu Ala Glu Ala Gly Glu
20 25 30

Val Arg Thr Arg Leu Arg Ser Tyr Gly Leu Pro Trp Asp Leu Ala Glu
35 40 45

Asp Gly Gly Arg Ala Gly Pro Ser Gly Leu Glu Thr Leu Thr Pro Tyr
50 55 60

Ser Pro Thr Pro Ser Phe Thr Trp Ser Asp Ala Arg Leu His Arg Gly
65 70 75 80

Leu Val Thr Leu Leu Thr Gly Glu Ile Val Asp Ala Phe Ser Leu Glu
85 90 95

Phe Arg Thr Leu Tyr Ala Ala Ser Cys Pro Leu Pro Pro Ala Pro Pro
100 105 110

Gln Lys Pro Ser Val Ile Gly Gly Leu Gln Arg Gly Arg Ser Pro His
115 120 125

Arg Val Ser Arg Arg Arg Ser Val Ala Pro Ala Ser Pro Pro Pro Pro
130 135 140

Asp Gly Pro Leu Ala His Arg Leu Ala Ala Cys Arg Val Ser Pro Ala
145 150 155 160

Thr Pro Gly Pro Ala Leu Ser Asp Ile Leu Arg Ser Val Gln Arg Ala
165 170 175

Arg Thr Pro Ser Gly Pro Pro Ala Arg Pro Ser Arg Ser Met Trp Asp
180 185 190

Leu Ser Arg Leu Ser Gln Leu Ser Gly Ser Ser Asp Gly Asp Asn Glu
195 200 205

Leu Lys Lys Ser Trp Gly Ser Lys Asp Thr Pro Ala Lys Ala Leu Met
210 215 220

Arg Gln Arg Gly Thr Gly Gly Gly Pro Trp Gly Glu Val Asp Ser Arg
225 230 235 240

Pro Pro Trp Gly Gly Ala Leu Pro Leu Pro Pro Ala His Arg Leu Arg
245 250 255

Tyr Leu Ser Pro Ala Arg Arg Arg Phe Gly Gly Asp Ala Thr Phe Lys
260 265 270

Leu Gln Glu Pro Arg Gly Val Arg Pro Ser Asp Trp Ala Pro Arg Ala
275 280 285

Gly Leu Gly Gly Gln Pro
290

<210> 141
<211> 90
<212> PRT
<213> Homo sapien

<400> 141

Met Ala Leu Gln Leu Ser Arg Glu Gln Gly Ile Thr Leu Arg Gly Ser
1 5 10 15

Ala Glu Ile Val Ala Glu Phe Phe Ser Phe Gly Ile Asn Ser Ile Leu
20 25 30

Tyr Gln Arg Gly Ile Tyr Pro Ser Glu Thr Phe Thr Arg Val Gln Lys
35 40 45

Tyr Gly Leu Thr Leu Leu Val Thr Thr Asp Leu Glu Leu Ile Lys Tyr
50 55 60

Leu Asn Asn Val Val Glu Gln Leu Lys Val His Pro Glu Lys Ser Leu
65 70 75 80

Arg Lys Leu Ser Arg Met Lys Ser Val Gln
85 90

<210> 142
<211> 373
<212> PRT
<213> Homo sapien

<400> 142

Arg Thr Val Thr Val Arg Thr Arg Ile Ala Val Leu Ser Leu Arg Pro
1 5 10 15

Gln Cys Gly Gly Ile Leu Phe Arg His Val Val Val Leu Thr Leu Gly
20 25 30

Asn Gly Leu Gly Gln Asn Leu Asp Leu Ala Ser Val Gln Ala His Ala
35 40 45

Ala Val Gln Gly Arg Arg Val Leu Ile Pro Gly Val Asn Ile Arg Gln
50 55 60

Glu Asn Leu Gly Arg Gly Arg Phe His Asp His Val Gln Asp Ala Ala
65 70 75 80

Val Gly Gly Val Gly Gln Ala Leu Arg Cys His Gln His Lys Ala Val
85 90 95

Gly Leu Thr Gln His Leu Glu Pro Phe Pro Asp Leu Arg Ala Glu Cys
100 105 110

Arg Val Ala Glu His Gln Pro Gly Phe Val Gln Asp Asp Glu Arg Pro
115 120 125

Pro Val Trp Trp Asn Ser Asn Pro Glu Lys Asp Ile Phe Val Val Arg
130 135 140

Glu Asn Gly Thr Thr Cys Leu Met Ala Glu Phe Ala Ala Lys Phe Ile
145 150 155 160

Val Pro Tyr Asp Val Trp Ala Ser Asn Tyr Val Asp Leu Ile Thr Glu
165 170 175

Gln Ala Asp Ile Ala Leu Thr Arg Gly Ala Glu Val Lys Gly Arg Cys
180 185 190

Gly His Ser Gln Ser Glu Leu Gln Val Phe Trp Val Asp Arg Ala Tyr
195 200 205

Ala Leu Lys Met Leu Phe Val Lys Glu Ser His Asn Met Ser Lys Gly
210 215 220

Pro Glu Ala Thr Trp Arg Leu Ser Lys Val Gln Phe Val Tyr Asp Ser
225 230 235 240

Ser Glu Lys Thr His Phe Lys Asp Ala Val Ser Ala Gly Lys His Thr
245 250 255

Ala Asn Ser His His Leu Ser Ala Leu Val Thr Pro Ala Gly Lys Ser
260 265 270

Tyr Glu Cys Gln Ala Gln Gln Thr Ile Ser Leu Ala Ser Ser Asp Pro
275 280 285

Gln Lys Thr Val Thr Met Ile Leu Ser Ala Val His Ile Gln Pro Phe
290 295 300

Asp Ile Ile Ser Asp Phe Val Phe Ser Glu Glu His Lys Cys Pro Val
305 310 315 320

Asp Glu Arg Glu Gln Leu Glu Glu Thr Leu Pro Leu Ile Leu Gly Leu
325 330 335

Ile Leu Gly Leu Val Ile Met Val Thr Leu Ala Ile Tyr His Val His
340 345 350

His Lys Met Thr Ala Asn Gln Val Gln Ile Pro Arg Asp Arg Ser Gln
355 360 365

Tyr Lys His Met Gly
370

<210> 143
<211> 148
<212> PRT
<213> Homo sapien

<400> 143

Gly Gly Leu Ser Pro Ile His Pro Glu Val Thr Val Tyr Pro Ala Lys
1 5 10 15

Thr Gln Pro Leu Gln His His Asn Leu Leu Val Cys Ser Val Ser Gly
20 25 30

Phe Tyr Pro Gly Ser Ile Glu Val Arg Trp Phe Arg Asn Gly Gln Glu
35 40 45

Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gln Asn Gly Asp Trp
50 55 60

Thr Phe Gln Thr Leu Val Met Leu Glu Thr Val Pro Arg Ser Gly Glu
65 70 75 80

Val Tyr Thr Cys Gln Val Glu His Pro Ser Val Met Ser Pro Leu Thr
85 90 95

Val Glu Trp Arg Ala Arg Ser Glu Ser Ala Gln Ser Lys Met Leu Ser
100 105 110

Gly Val Gly Gly Phe Val Leu Gly Leu Leu Phe Leu Gly Ala Gly Leu
115 120 125

Phe Ile Tyr Phe Arg Asn Gln Lys Gly His Ser Gly Leu Gln Pro Thr
130 135 140

Gly Phe Leu Ser
145

<210> 144
<211> 72
<212> PRT
<213> Homo sapien

<400> 144

Met Val Leu Ser Ser Pro Leu Ala Leu Ala Gly Asp Thr Gln Pro Arg
1 5 10 15

Phe Leu Trp Gln Asp Lys Tyr Gly Val Ser Phe Leu Gln Arg Asp Gly
20 25 30

Ala Gly Ala Val Ser Trp Lys Glu Cys Ile Tyr Asn Gln Glu Glu Phe
35 40 45

Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val Thr Glu Leu
50 55 60

Gly Arg Pro Val Ala Asp Pro Ser
65 70

<210> 145
<211> 191
<212> PRT
<213> Homo sapien

<400> 145

Asp Ser Pro Ala Pro Leu Ala Pro Gly Pro Val Leu Phe Ser Ser Met
1 5 10 15

Val Cys Leu Lys Leu Pro Gly Gly Ser Cys Met Ala Ala Leu Thr Val
20 25 30

Thr Leu Met Val Leu Ser Ser Pro Leu Ala Leu Ala Gly Asp Thr Gln
35 40 45

Leu His Pro Glu Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln
50 55 60

His His Asn Leu Leu Val Cys Ser Val Ser Gly Phe Tyr Pro Gly Ser
65 70 75 80

Ile Glu Val Arg Trp Phe Arg Asn Gly Gln Glu Glu Lys Ala Gly Val
85 90 95

Val Ser Thr Gly Leu Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu
100 105 110

Val Met Leu Glu Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln
115 120 125

Val Glu His Pro Ser Val Met Ser Pro Leu Thr Val Glu Trp Arg Ala

130 135 140

Arg Ser Glu Ser Ala Gln Ser Lys Met Leu Ser Gly Val Gly Gly Phe
145 150 155 160

Val Leu Gly Leu Leu Phe Leu Gly Ala Gly Leu Phe Ile Tyr Phe Arg
165 170 175

Asn Gln Lys Gly His Ser Gly Leu Gln Pro Thr Gly Phe Leu Ser
180 185 190

<210> 146
<211> 112
<212> PRT
<213> Homo sapien

<400> 146

Met Val Leu Ser Ser Pro Leu Ala Leu Ala Gly Asp Thr Gln Leu His
1 5 10 15

Pro Glu Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His
20 25 30

Asn Leu Leu Val Cys Ser Val Ser Gly Phe Tyr Pro Gly Ser Ile Glu
35 40 45

Val Arg Trp Phe Arg Asn Gly Gln Glu Glu Lys Ala Gly Val Val Ser
50 55 60

Thr Gly Leu Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val Met
65 70 75 80

Leu Glu Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Gly Gly
85 90 95

Ala Pro Lys Cys Asp Glu Pro Ser His Ser Gly Met Glu Ser Thr Val
100 105 110

<210> 147
<211> 128
<212> PRT
<213> Homo sapien

<400> 147

Gly Phe Arg Gly Pro Ala His Trp Pro Leu Pro Thr Gly Leu His Leu
1 5 10 15

Thr Pro Pro Ser Leu Ser Val Pro Ser Phe Ala Ile Asn Phe Lys Val
20 25 30

Gly Ser Ser Gly Asp Ile Ala Leu His Ile Asn Pro Arg Met Gly Asn
35 40 45

Gly Thr Val Val Arg Asn Ser Leu Leu Asn Gly Ser Trp Gly Ser Glu
50 55 60

Glu Lys Lys Ile Thr His Asn Pro Phe Gly Pro Gly Gln Phe Phe Asp
65 70 75 80

Leu Ser Ile Arg Cys Gly Leu Asp Arg Phe Lys Val Tyr Ala Asn Gly
85 90 95

Gln His Leu Phe Asp Phe Ala His Arg Leu Ser Ala Phe Gln Arg Val
100 105 110

Asp Thr Leu Glu Ile Gln Gly Asp Val Thr Leu Ser Tyr Val Gln Ile
115 120 125

<210> 148
<211> 256
<212> PRT
<213> Homo sapien

<400> 148

Met Ala Ala Thr Cys Glu Ile Ser Asn Ile Phe Ser Asn Tyr Phe Ser
1 5 10 15

Ala Met Tyr Ser Ser Glu Asp Ser Thr Leu Ala Ser Val Pro Pro Ala
20 25 30

Ala Thr Phe Gly Ala Asp Asp Leu Val Leu Thr Leu Ser Asn Pro Gln
35 40 45

Met Ser Leu Glu Gly Thr Glu Lys Ala Ser Trp Leu Gly Glu Gln Pro
50 55 60

Gln Phe Trp Ser Lys Thr Gln Val Leu Asp Trp Ile Ser Tyr Gln Val
65 70 75 80

Glu Lys Asn Lys Tyr Asp Ala Ser Ala Ile Asp Phe Ser Arg Cys Asp
85 90 95

Met Asp Gly Ala Thr Leu Cys Asn Cys Ala Leu Glu Glu Leu Arg Leu
100 105 110

Val Phe Gly Pro Leu Gly Asp Gln Leu His Ala Gln Leu Arg Asp Leu
115 120 125

Thr Ser Ser Ser Ser Asp Glu Leu Ser Trp Ile Ile Glu Leu Leu Glu
130 135 140

Lys Asp Gly Met Ala Phe Gln Glu Ala Leu Asp Pro Gly Pro Phe Asp
145 150 155 160

Gln Gly Ser Pro Phe Ala Gln Glu Leu Leu Asp Asp Gly Gln Gln Ala
165 170 175

Ser Pro Tyr His Pro Gly Ser Cys Gly Ala Gly Ala Pro Ser Pro Gly
180 185 190

Ser Ser Asp Val Ser Thr Ala Gly Thr Gly Ala Ser Arg Ser Ser His
195 200 205

Ser Ser Asp Ser Gly Gly Ser Asp Val Asp Leu Asp Pro Thr Asp Gly
210 215 220

Lys Leu Phe Pro Ser Gly Glu Ser Arg Glu Val Pro Lys Arg Ala Ser
225 230 235 240

His Leu Ala Met His Arg Gly Pro Gly Ser Ser Cys Ser Leu Phe Leu
245 250 255

<210> 149
<211> 250
<212> PRT
<213> Homo sapien

<400> 149

Gly Ser Ala Ala Ala Arg Tyr Leu Ser Ala Thr Trp Arg Asn Trp Ile
1 5 10 15

Ser Leu Pro Pro Ala Gly Leu Pro Ala Thr Ala Gly Leu Arg His Ser
20 25 30

Gly Ser Leu Met Ala Ala Thr Cys Glu Ile Ser Asn Ile Phe Ser Asn
35 40 45

Tyr Phe Ser Ala Met Tyr Ser Ser Glu Asp Ser Thr Leu Ala Ser Val
50 55 60

Pro Pro Ala Ala Thr Phe Gly Ala Asp Asp Leu Val Leu Thr Leu Ser
65 70 75 80

Asn Pro Gln Met Ser Leu Glu Gly Thr Glu Lys Ala Ser Trp Leu Gly
85 90 95

Glu Gln Pro Gln Phe Trp Ser Lys Thr Gln Val Leu Asp Trp Ile Ser
100 105 110

Tyr Gln Val Glu Lys Asn Lys Tyr Asp Ala Ser Ala Ile Asp Phe Ser
115 120 125

Arg Cys Asp Met Asp Gly Ala Thr Leu Cys Asn Cys Ala Leu Glu Glu
130 135 140

Leu Arg Leu Val Phe Gly Pro Leu Gly Asp Gln Leu His Ala Gln Leu
145 150 155 160

Arg Asp Leu Thr Ser Ser Ser Ser Asp Glu Leu Ser Trp Ile Ile Glu
165 170 175

Leu Leu Glu Lys Asp Gly Met Ala Phe Gln Glu Ala Leu Asp Pro Gly
180 185 190

Pro Phe Asp Gln Gly Ser Pro Phe Ala Gln Glu Leu Leu Asp Asp Gly
195 200 205

Gln Gln Ala Ser Pro Tyr His Pro Gly Ser Cys Gly Ala Gly Ala Pro
210 215 220

Ser Pro Gly Ser Ser Asp Val Ser Thr Ala Gly Thr Gly Thr Gly Trp
225 230 235 240

Glu Val Cys Pro Glu Ser Gln Gln Arg Gly
245 250

<210> 150
<211> 402
<212> PRT
<213> Homo sapien

<400> 150

Met Ala Ala Thr Cys Glu Ile Ser Asn Ile Phe Ser Asn Tyr Phe Ser
1 5 10 15

Ala Met Tyr Ser Ser Glu Asp Ser Thr Leu Ala Ser Val Pro Pro Ala
20 25 30

Ala Thr Phe Gly Ala Asp Asp Leu Val Leu Thr Leu Ser Asn Pro Gln
35 40 45

Met Ser Leu Glu Gly Thr Glu Lys Ala Ser Trp Leu Gly Glu Gln Pro
50 55 60

Gln Phe Trp Ser Lys Thr Gln Val Leu Asp Trp Ile Ser Tyr Gln Val
65 70 75 80

Glu Lys Asn Lys Tyr Asp Ala Ser Ala Ile Asp Phe Ser Arg Cys Asp
85 90 95

Met Asp Gly Ala Thr Leu Cys Asn Cys Ala Leu Glu Glu Leu Arg Leu
100 105 110

Val Phe Gly Pro Leu Gly Asp Gln Leu His Ala Gln Leu Arg Asp Leu
115 120 125

Thr Ser Ser Ser Ser Asp Glu Leu Ser Trp Ile Ile Glu Leu Leu Glu
130 135 140

Lys Asp Gly Met Ala Phe Gln Glu Ala Leu Asp Pro Gly Pro Phe Asp
145 150 155 160

Gln Gly Ser Pro Phe Ala Gln Glu Leu Leu Asp Asp Gly Gln Gln Ala
165 170 175

Ser Pro Tyr His Pro Gly Ser Cys Gly Ala Gly Ala Pro Ser Pro Gly
180 185 190

Ser Ser Asp Val Ser Thr Ala Gly Thr Gly Thr Gly Trp Glu Val Cys
195 200 205

Pro Glu Ser Arg Ser Val Val Glu Gln Arg Val Gly Arg Gln Gly Thr
210 215 220

Tyr Ser Asp Pro Ala Pro Arg Thr Gly Ala Ser Arg Ser Ser His Ser
225 230 235 240

Ser Asp Ser Gly Gly Ser Asp Val Asp Leu Asp Pro Thr Asp Gly Lys
245 250 255

Leu Phe Pro Ser Asp Gly Phe Arg Asp Cys Lys Lys Gly Asp Pro Lys
260 265 270

His Gly Lys Arg Lys Arg Gly Arg Pro Arg Lys Leu Ser Lys Glu Tyr
275 280 285

Trp Asp Cys Leu Glu Gly Lys Lys Ser Lys His Ala Pro Arg Gly Thr
290 295 300

His Leu Trp Glu Phe Ile Arg Asp Ile Leu Ile His Pro Glu Leu Asn
305 310 315 320

Glu Gly Leu Met Lys Trp Glu Asn Arg His Glu Gly Val Phe Lys Phe
325 330 335

Leu Arg Ser Glu Ala Val Ala Gln Leu Trp Gly Gln Lys Lys Lys Asn
340 345 350

Ser Asn Met Thr Tyr Glu Lys Leu Ser Arg Ala Met Arg Tyr Tyr Tyr
355 360 365

Lys Arg Glu Ile Leu Glu Arg Val Asp Gly Arg Arg Leu Val Tyr Lys
370 375 380

Phe Gly Lys Asn Ser Ser Gly Trp Lys Glu Glu Glu Val Leu Gln Ser
385 390 395 400

Arg Asn

<210> 151
<211> 219
<212> PRT
<213> Homo sapien

<400> 151

Met Ser Leu Pro Val Lys Pro Glu Leu Leu Gly Asp Leu Glu Ile Pro
1 5 10 15

Ala Val Pro Ile Leu His Ser Met Val Gln Lys Phe Pro Gly Val Ser
20 25 30

Phe Gly Ile Ser Thr Asp Ser Glu Val Leu Thr His Tyr Asn Ile Thr
35 40 45

Gly Asn Thr Ile Cys Leu Phe Arg Leu Val Asp Asn Glu Gln Leu Asn
50 55 60

Leu Glu Asp Glu Asp Ile Glu Ser Ile Asp Ala Thr Lys Leu Ser Arg

65 70 75 80

Phe Ile Glu Ile Asn Ser Leu His Met Val Thr Glu Tyr Asn Pro Val
85 90 95

Thr Val Ile Gly Leu Phe Asn Ser Val Ile Gln Ile His Leu Leu Leu
100 105 110

Ile Met Asn Lys Ala Ser Pro Glu Tyr Glu Glu Asn Met His Arg Tyr
115 120 125

Gln Lys Ala Ala Lys Leu Phe Gln Gly Lys Ile Leu Phe Ile Leu Val
130 135 140

Asp Ser Gly Met Lys Glu Asn Gly Lys Val Ile Ser Phe Phe Lys Leu
145 150 155 160

Lys Glu Ser Gln Leu Pro Ala Leu Ala Ile Tyr Gln Thr Leu Asp Asp
165 170 175

Glu Trp Asp Thr Leu Pro Thr Ala Glu Val Ser Val Glu His Val Gln
180 185 190

Asn Phe Cys Asp Gly Phe Leu Ser Gly Lys Leu Leu Lys Glu Asn Arg
195 200 205

Glu Ser Glu Gly Lys Thr Pro Lys Val Glu Leu
210 215

<210> 152
<211> 172
<212> PRT
<213> Homo sapien

<400> 152

Met Lys Glu Thr Cys Gln Leu Glu Ile Gln Val Asp Asn Glu Gln Leu
1 5 10 15

Asn Leu Glu Asp Glu Asp Ile Glu Ser Ile Asp Ala Thr Lys Leu Ser
20 25 30

Arg Phe Ile Glu Ile Asn Ser Leu His Met Val Thr Glu Tyr Asn Pro
35 40 45

Val Thr Val Ile Gly Leu Phe Asn Ser Val Ile Gln Ile His Leu Leu
50 55 60

Leu Ile Met Asn Lys Ala Ser Pro Glu Tyr Glu Glu Asn Met His Arg
65 70 75 80

Tyr Gln Lys Ala Ala Lys Leu Phe Gln Gly Lys Ile Leu Phe Ile Leu
85 90 95

Val Asp Ser Gly Met Lys Glu Asn Gly Lys Val Ile Ser Phe Phe Lys
100 105 110

Leu Lys Glu Ser Gln Leu Pro Ala Leu Ala Ile Tyr Gln Thr Leu Asp
115 120 125

Asp Glu Trp Asp Thr Leu Pro Thr Ala Glu Val Ser Val Glu His Val
130 135 140

Gln Asn Phe Cys Asp Gly Phe Leu Ser Gly Lys Leu Leu Lys Glu Asn
145 150 155 160

Arg Glu Ser Glu Gly Lys Thr Pro Lys Val Glu Leu
165 170

<210> 153
<211> 329
<212> PRT
<213> Homo sapien

<400> 153

Ser Gly Asp Leu Gln Pro His Ser Arg Cys Pro Gly Gly Arg Arg Asp
1 5 10 15

Pro Gln Ile Lys Leu Ser Leu Thr Glu Lys Asp Glu Gly Gln Glu Glu
20 25 30

Cys Ser Phe Leu Val Ala Leu Met Gln Lys Asp Arg Arg Lys Leu Lys
35 40 45

Arg Phe Gly Ala Asn Val Leu Thr Ile Gly Tyr Ala Ile Tyr Glu Cys
50 55 60

Pro Asp Lys Asp Glu His Leu Asn Lys Asp Phe Phe Arg Tyr His Ala
65 70 75 80

Ser Arg Ala Arg Ser Lys Thr Phe Ile Asn Leu Arg Glu Val Ser Asp
85 90 95

Arg Phe Lys Leu Pro Pro Gly Glu Tyr Ile Leu Ile Pro Ser Thr Phe

100 105 110

Glu Pro His Gln Glu Ala Asp Phe Cys Leu Arg Ile Phe Ser Glu Lys
115 120 125

Lys Ala Ile Thr Arg Asp Met Asp Gly Asn Val Asp Ile Asp Leu Pro
130 135 140

Glu Pro Pro Lys Pro Thr Pro Pro Asp Gln Glu Thr Glu Glu Glu Gln
145 150 155 160

Arg Phe Arg Ala Leu Phe Glu Gln Val Ala Gly Glu Asp Met Glu Val
165 170 175

Thr Ala Glu Glu Leu Glu Tyr Val Leu Asn Ala Val Leu Gln Lys Lys
180 185 190

Lys Asp Ile Lys Phe Lys Lys Leu Ser Leu Ile Ser Cys Lys Asn Ile
195 200 205

Ile Ser Leu Met Asp Thr Ser Gly Asn Gly Lys Leu Glu Phe Asp Glu
210 215 220

Phe Lys Val Phe Trp Asp Lys Leu Lys Gln Trp Ile Asn Leu Phe Leu
225 230 235 240

Arg Phe Asp Ala Asp Lys Ser Gly Thr Met Ser Thr Tyr Glu Leu Arg
245 250 255

Thr Ala Leu Lys Ala Ala Gly Phe Gln Leu Ser Ser His Leu Leu Gln
260 265 270

Leu Ile Val Leu Arg Tyr Ala Asp Glu Glu Leu Gln Leu Asp Phe Asp
275 280 285

Asp Phe Leu Asn Cys Leu Val Arg Leu Glu Asn Ala Ser Arg Val Phe
290 295 300

Gln Ala Leu Ser Thr Lys Asn Lys Glu Phe Ile His Leu Asn Ile Asn
305 310 315 320

Glu Phe Ile His Leu Thr Met Asn Ile
325

<210> 154
<211> 595

<212> PRT
<213> Homo sapien

<400> 154

Met Val Cys Leu Phe Leu Lys Cys Asn Leu Gln Asn Ser Pro Glu Arg
1 5 10 15

Asn Asn Ser Phe Trp Glu Val Val Ala Ala Ala Gly Thr Val Ala Pro
20 25 30

Trp Glu Ile Val Lys Asn Pro Glu Phe Ile Leu Gly Gly Ala Thr Arg
35 40 45

Thr Asp Ile Cys Gln Gly Glu Leu Gly Asp Cys Trp Leu Leu Ala Ala
50 55 60

Ile Ala Ser Leu Thr Leu Asn Gln Lys Ala Leu Ala Arg Val Ile Pro
65 70 75 80

Gln Asp Gln Ser Phe Gly Pro Gly Tyr Ala Gly Ile Phe His Phe Gln
85 90 95

Phe Trp Gln His Ser Glu Trp Leu Asp Val Val Ile Asp Asp Arg Leu
100 105 110

Pro Thr Phe Arg Asp Arg Leu Val Phe Leu His Ser Ala Asp His Asn
115 120 125

Glu Phe Trp Ser Ala Leu Leu Glu Lys Ala Tyr Ala Lys Leu Asn Gly
130 135 140

Ser Tyr Glu Ala Leu Lys Gly Gly Ser Ala Ile Glu Ala Met Glu Asp
145 150 155 160

Phe Thr Gly Gly Val Ala Glu Thr Phe Gln Thr Lys Glu Ala Pro Glu
165 170 175

Asn Phe Tyr Glu Ile Leu Glu Lys Ala Leu Lys Arg Gly Ser Leu Leu
180 185 190

Gly Cys Phe Ile Asp Thr Arg Ser Ala Ala Glu Ser Glu Ala Arg Thr
195 200 205

Pro Phe Gly Leu Ile Lys Gly His Ala Tyr Ser Val Thr Gly Ile Asp
210 215 220

Gln Val Ser Phe Arg Gly Gln Arg Ile Glu Leu Ile Arg Ile Arg Asn
225 230 235 240

Pro Trp Gly Gln Val Glu Trp Asn Gly Ser Trp Ser Asp Arg Met Ala
245 250 255

Phe Lys Asp Phe Lys Ala His Phe Asp Lys Val Glu Ile Cys Asn Leu
260 265 270

Thr Pro Asp Ala Leu Glu Glu Asp Ala Asp Pro Gln Ile Lys Leu Ser
275 280 285

Leu Thr Glu Lys Asp Glu Gly Gln Glu Glu Cys Ser Phe Leu Val Ala
290 295 300

Leu Met Gln Lys Asp Arg Arg Lys Leu Lys Arg Phe Gly Ala Asn Val
305 310 315 320

Leu Thr Ile Gly Tyr Ala Ile Tyr Glu Cys Pro Asp Lys Asp Glu His
325 330 335

Leu Asn Lys Asp Phe Phe Arg Tyr His Ala Ser Arg Ala Arg Ser Lys
340 345 350

Thr Phe Ile Asn Leu Arg Glu Val Ser Asp Arg Phe Lys Leu Pro Pro
355 360 365

Gly Glu Tyr Ile Leu Ile Pro Ser Thr Phe Glu Pro His Gln Glu Ala
370 375 380

Asp Phe Cys Leu Arg Ile Phe Ser Glu Lys Lys Ala Ile Thr Arg Asp
385 390 395 400

Met Asp Gly Asn Val Asp Ile Asp Leu Pro Glu Pro Pro Lys Pro Thr
405 410 415

Pro Pro Asp Gln Glu Thr Glu Glu Glu Gln Arg Phe Arg Ala Leu Phe
420 425 430

Glu Gln Val Ala Gly Glu Asp Met Glu Val Thr Ala Glu Glu Leu Glu
435 440 445

Tyr Val Leu Asn Ala Val Leu Gln Lys Lys Lys Asp Ile Lys Phe Lys
450 455 460

Lys Leu Ser Leu Ile Ser Cys Lys Asn Ile Ile Ser Leu Met Asp Thr

465 470 475 480

Ser Gly Asn Gly Lys Leu Glu Phe Asp Glu Phe Lys Val Phe Trp Asp
485 490 495

Lys Leu Lys Gln Trp Ile Asn Leu Phe Leu Arg Phe Asp Ala Asp Lys
500 505 510

Ser Gly Thr Met Ser Thr Tyr Glu Leu Arg Thr Ala Leu Lys Ala Ala
515 520 525

Gly Phe Gln Leu Ser Ser His Leu Leu Gln Leu Ile Val Leu Arg Tyr
530 535 540

Ala Asp Glu Glu Leu Gln Leu Asp Phe Asp Asp Phe Leu Asn Cys Leu
545 550 555 560

Val Arg Leu Glu Asn Ala Ser Arg Val Phe Gln Ala Leu Ser Thr Lys
565 570 575

Asn Lys Glu Phe Ile His Leu Asn Ile Asn Glu Phe Ile His Leu Thr
580 585 590

Met Asn Ile
595

<210> 155
<211> 85
<212> PRT
<213> Homo sapien

<400> 155

Ala Leu Ser Val Val Ala Ala Glu Val Arg Val Val Gly Arg Asn Gly
1 5 10 15

Glu Ser Ser Glu Leu Asp Leu Gln Gly Ile Arg Ile Asp Ser Asp Ile
20 25 30

Ser Gly Thr Leu Lys Phe Ala Cys Glu Ser Ile Val Glu Glu Tyr Glu
35 40 45

Asp Glu Leu Ile Glu Phe Phe Ser Arg Glu Ala Asp Asn Val Lys Asp
50 55 60

Lys Leu Cys Ser Lys Arg Thr Asp Leu Cys Asp His Ala Leu His Ile
65 70 75 80

Ser His Asp Glu Leu
85

<210> 156
<211> 255
<212> PRT
<213> Homo sapien

<400> 156

Met Ala Asp Tyr Ser Thr Val Pro Pro Pro Ser Ser Gly Ser Ala Gly
1 5 10 15

Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Val Asn Asp Ala Phe Lys
20 25 30

Asp Ala Leu Gln Arg Ala Arg Gln Ile Ala Ala Lys Ile Gly Gly Asp
35 40 45

Ala Gly Thr Ser Leu Asn Ser Asn Asp Tyr Gly Tyr Gly Gly Gln Lys
50 55 60

Arg Pro Leu Glu Asp Gly Asp Gln Pro Asp Ala Lys Lys Val Ala Pro
65 70 75 80

Gln Asn Asp Ser Phe Gly Thr Gln Leu Pro Pro Met His Gln Gln Gln
85 90 95

Ser Arg Ser Val Met Thr Glu Glu Tyr Lys Val Pro Asp Gly Met Val
100 105 110

Gly Phe Ile Ile Gly Arg Gly Gly Glu Gln Ile Ser Arg Ile Gln Gln
115 120 125

Glu Ser Gly Cys Lys Ile Gln Ile Ala Pro Asp Ser Gly Gly Leu Pro
130 135 140

Glu Arg Ser Cys Met Leu Thr Gly Thr Pro Glu Ser Val Gln Ser Ala
145 150 155 160

Lys Arg Leu Leu Asp Gln Ile Val Glu Lys Gly Arg Pro Ala Pro Gly
165 170 175

Phe His His Gly Asp Gly Pro Gly Asn Ala Val Gln Glu Ile Met Ile
180 185 190

Pro Ala Ser Lys Ala Gly Leu Val Ile Gly Lys Gly Gly Glu Thr Ile

195 200 205

Lys Gln Leu Gln Glu Arg Ala Gly Val Lys Met Val Met Ile Gln Asp
210 215 220

Gly Val Ala Ala Ala Ala Ala Val Phe Phe Thr Ser Ile Ile Arg Leu
225 230 235 240

Ala Phe Asn Lys Glu Lys Val Leu Thr Pro Val Leu Asn Cys Thr
245 250 255

<210> 157
<211> 174
<212> PRT
<213> Homo sapien

<400> 157

Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys
1 5 10 15

Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met
20 25 30

Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp
35 40 45

Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn
50 55 60

Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Lys Gln Lys Ala
65 70 75 80

His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile
85 90 95

Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly
100 105 110

Leu Glu Leu Ala Ala Met Ile Val Ser Met Tyr Leu Tyr Leu Pro Gly
115 120 125

Arg Pro Ala Trp Ser Arg Pro Arg Tyr Ser Asp Ser Val Gly Arg Val
130 135 140

Ser Phe Pro Ser Leu Val Cys Phe Leu Met Arg Leu Glu Ala Met Ala
145 150 155 160

Lys Thr Phe Arg Asn Ser Leu Arg Met Glu Lys Asp Ser Thr
165 170

<210> 158
<211> 354
<212> PRT
<213> Homo sapien

<400> 158

Met Gly Gln Asp Trp Gly Pro His His Met Ser Arg Glu Asp Leu Ile
1 5 10 15

Cys Gly Gly Gly Lys Gly Ser Leu Val Trp Pro Thr Trp Ser Thr Thr
20 25 30

Ser Leu Trp Pro Gln Val Leu Leu Val Gln Phe Lys Gly Thr Gly Lys
35 40 45

Tyr Tyr Ala Ile Lys Ala Leu Lys Lys Gln Glu Val Leu Ser Arg Asp
50 55 60

Glu Ile Glu Ser Leu Tyr Cys Glu Lys Arg Ile Leu Glu Ala Val Gly
65 70 75 80

Cys Thr Gly His Pro Phe Leu Leu Ser Leu Leu Ala Cys Phe Gln Thr
85 90 95

Ser Ser His Ala Cys Phe Val Thr Glu Phe Val Pro Gly Gly Asp Leu
100 105 110

Met Met Gln Ile His Glu Asp Val Phe Pro Glu Pro Gln Ala Arg Phe
115 120 125

Tyr Val Ala Cys Val Val Leu Gly Leu Gln Phe Leu His Glu Lys Lys
130 135 140

Ile Ile Tyr Arg Asp Leu Lys Leu Asp Asn Leu Leu Leu Asp Ala Gln
145 150 155 160

Gly Phe Leu Lys Ile Ala Asp Phe Gly Leu Cys Lys Glu Gly Ile Gly
165 170 175

Phe Gly Asp Arg Thr Ser Thr Phe Cys Gly Thr Pro Glu Phe Leu Ala
180 185 190

Pro Glu Val Leu Thr Gln Glu Ala Tyr Thr Arg Ala Val Asp Trp Trp

195 200 205

Gly Leu Gly Val Leu Leu Tyr Glu Met Leu Val Gly Glu Cys Pro Phe
210 215 220

Pro Gly Asp Thr Glu Glu Glu Val Phe Asp Cys Ile Val Asn Met Asp
225 230 235 240

Ala Pro Tyr Pro Gly Phe Leu Ser Val Gln Gly Leu Glu Phe Ile Gln
245 250 255

Lys Leu Leu Gln Lys Cys Pro Glu Lys Arg Leu Gly Ala Gly Glu Gln
260 265 270

Asp Ala Glu Glu Ile Lys Val Gln Pro Phe Phe Arg Thr Thr Asn Trp
275 280 285

Gln Ala Leu Leu Ala Arg Thr Ile Gln Pro Pro Phe Val Pro Thr Leu
290 295 300

Cys Gly Pro Ala Asp Leu Arg Tyr Phe Glu Gly Glu Phe Thr Gly Leu
305 310 315 320

Pro Pro Ala Leu Thr Pro Pro Ala Pro His Ser Leu Leu Thr Ala Arg
325 330 335

Gln Gln Ala Ala Phe Arg Asp Phe Asp Phe Val Ser Glu Arg Phe Leu
340 345 350

Glu Pro

<210> 159
<211> 489
<212> PRT
<213> Homo sapien

<400> 159

Met Glu Glu Gly Ala Pro Arg Gln Pro Gly Pro Ser Gln Trp Pro Pro
1 5 10 15

Glu Asp Glu Lys Glu Val Ile Arg Arg Ala Ile Gln Lys Glu Leu Lys
20 25 30

Ile Lys Glu Gly Val Glu Asn Leu Arg Arg Val Ala Thr Asp Arg Arg
35 40 45

His Leu Gly His Val Gln Gln Leu Leu Arg Ser Ser Asn Arg Arg Leu
50 55 60

Glu Gln Leu His Gly Glu Leu Arg Glu Leu His Ala Arg Ile Leu Leu
65 70 75 80

Pro Gly Pro Gly Pro Gly Pro Ala Glu Pro Val Ala Ser Gly Pro Arg
85 90 95

Pro Trp Ala Glu Gln Leu Arg Ala Arg His Leu Glu Ala Leu Arg Arg
100 105 110

Gln Leu His Val Glu Leu Lys Val Lys Gln Gly Ala Glu Asn Met Thr
115 120 125

His Thr Cys Ala Ser Gly Thr Pro Lys Glu Arg Lys Leu Leu Ala Ala
130 135 140

Ala Gln Gln Met Leu Arg Asp Ser Gln Leu Lys Val Ala Leu Leu Arg
145 150 155 160

Met Lys Ile Ser Ser Leu Glu Ala Ser Gly Ser Pro Glu Pro Gly Pro
165 170 175

Glu Leu Leu Ala Glu Glu Leu Gln His Arg Leu His Val Glu Ala Ala
180 185 190

Val Ala Glu Gly Ala Lys Asn Val Val Lys Leu Leu Ser Ser Arg Arg
195 200 205

Thr Gln Asp Arg Lys Ala Leu Ala Glu Ala Gln Ala Gln Leu Gln Glu
210 215 220

Ser Ser Gln Lys Leu Asp Leu Leu Arg Leu Ala Leu Glu Gln Leu Leu
225 230 235 240

Glu Gln Leu Pro Pro Ala His Pro Leu Arg Ser Arg Val Thr Arg Glu
245 250 255

Leu Arg Ala Ala Val Pro Gly Tyr Pro Gln Pro Ser Gly Thr Pro Val
260 265 270

Lys Pro Thr Ala Leu Thr Gly Thr Leu Gln Val Arg Leu Leu Gly Cys
275 280 285

Glu Gln Leu Leu Thr Ala Val Pro Gly Arg Ser Pro Ala Ala Ala Leu
290 295 300

Ala Ser Ser Pro Ser Glu Gly Trp Leu Arg Thr Lys Ala Lys His Gln
305 310 315 320

Arg Gly Arg Gly Glu Leu Ala Ser Glu Val Leu Ala Val Leu Lys Val
325 330 335

Asp Asn Arg Val Val Gly Gln Thr Gly Trp Gly Gln Val Ala Glu Gln
340 345 350

Ser Trp Asp Gln Thr Phe Val Ile Pro Leu Glu Arg Ala Arg Glu Leu
355 360 365

Glu Ile Gly Val His Trp Arg Asp Trp Arg Gln Leu Cys Gly Val Ala
370 375 380

Phe Leu Arg Leu Glu Asp Phe Leu Asp Asn Ala Cys His Gln Leu Ser
385 390 395 400

Leu Ser Leu Val Pro Gln Gly Leu Leu Phe Ala Gln Val Thr Phe Cys
405 410 415

Asp Pro Val Ile Glu Arg Arg Pro Arg Leu Gln Arg Gln Glu Arg Ile
420 425 430

Phe Ser Lys Arg Arg Gly Arg Leu Pro Gly Leu Arg Leu Cys Val Arg
435 440 445

Ala Ile Pro Gly Thr Leu Arg Ala Ser Pro Gly Thr Ser Val Pro Phe
450 455 460

Pro His Arg Leu Leu Glu Pro Leu Leu Val His Pro Cys Ala Leu Pro
465 470 475 480

Gly Gly Pro Gly Leu Ala Gly Tyr Phe
485

<210> 160
<211> 287
<212> PRT
<213> Homo sapien

<400> 160

Met Asp Met Ala Trp Gln Met Met Gln Leu Leu Leu Leu Ala Leu Val
1 5 10 15

Thr Ala Ala Gly Ser Ala Gln Pro Arg Ser Ala Arg Ala Arg Thr Asp
20 25 30

Leu Leu Asn Val Cys Met Asn Ala Lys His His Lys Thr Gln Pro Ser
35 40 45

Pro Glu Asp Glu Leu Tyr Gly Gln Val Gly Ala Pro Gln Gly Pro Ser
50 55 60

Pro Gly Ser Val Pro Leu Asp Asp Leu Pro Gly Ala Glu Glu Pro Glu
65 70 75 80

Tyr Gly Gly Asp Gly Cys Gly Gly Glu Arg Leu Ser Pro Val Ser Ser
85 90 95

Pro Pro Ser Ala Val Pro Gly Arg Arg Met Pro Ala Ala Arg Pro Ala
100 105 110

Pro Ala Arg Ser Cys Thr Arg Thr Pro Pro Ala Cys Thr Thr Leu Thr
115 120 125

Gly Ile Thr Val Val Arg Trp Asn Pro Pro Ala Ser Ala Thr Leu Ser
130 135 140

Arg Thr Ala Val Ser Glu Cys Ser Pro Asn Leu Gly Pro Trp Ile Arg
145 150 155 160

Gln Val Asn Gln Ser Trp Arg Lys Glu Arg Ile Leu Asn Val Pro Leu
165 170 175

Cys Lys Glu Asp Cys Glu Arg Trp Trp Glu Asp Cys Arg Thr Ser Tyr
180 185 190

Thr Cys Lys Ser Asn Trp His Lys Gly Trp Asn Trp Thr Ser Gly Ile
195 200 205

Asn Glu Cys Pro Ala Gly Ala Leu Cys Ser Thr Phe Glu Ser Tyr Phe
210 215 220

Pro Thr Pro Ala Ala Leu Cys Glu Gly Leu Trp Ser His Ser Phe Lys
225 230 235 240

Val Ser Asn Tyr Ser Arg Gly Ser Gly Arg Cys Ile Gln Met Trp Phe
245 250 255

Asp Ser Ala Gln Gly Asn Pro Asn Glu Glu Val Ala Lys Phe Tyr Ala
260 265 270

Ala Ala Met Asn Ala Gly Ala Pro Ser Arg Gly Ile Ile Asp Ser
275 280 285

<210> 161
<211> 143
<212> PRT
<213> Homo sapien

<400> 161

Met Thr His Ser Leu Val Cys Pro Glu Thr Val Ser Arg Val Ser Ser
1 5 10 15

Val Leu Asn Arg Asn Thr Arg Gln Phe Gly Lys Lys His Leu Phe Asp
20 25 30

Gln Asp Glu Glu Thr Cys Trp Asn Ser Asp Gln Gly Pro Ser Gln Trp
35 40 45

Val Thr Leu Glu Phe Pro Gln Leu Ile Arg Val Ser Gln Leu Gln Ile
50 55 60

Gln Phe Gln Gly Gly Phe Ser Ser Arg Arg Gly Cys Leu Glu Gly Ser
65 70 75 80

Gln Gly Thr Gln Ala Leu His Lys Ile Val Asp Phe Tyr Pro Glu Asp
85 90 95

Asn Asn Ser Leu Gln Asp Ile Leu Pro Leu Leu Leu Gly Trp Val Val
100 105 110

Cys Ala Ser Gly Ser Phe Gly Leu Thr Gln Thr Arg Met Gly Thr Leu
115 120 125

Met Cys Asp Leu Glu His Val Thr Ser Arg Thr Pro Leu Phe Leu
130 135 140

<210> 162
<211> 116
<212> PRT
<213> Homo sapien

<400> 162

Gly Leu Ser Pro Pro Gly Ser Pro Pro Gly Ser Thr Ala Lys Ser Leu
1 5 10 15

Ile Leu His Arg Arg Phe Ile Gly Ser Ser Trp Glu Gly Ser Pro Pro
20 25 30

Thr Thr Cys Pro Glu Ala Ala Phe Glu Val Ser Ser Gly Phe Pro Gln
35 40 45

Leu Trp Leu Thr Ile Leu Phe Pro Glu Cys Leu Ser Pro Gly Arg Arg
50 55 60

Leu His Ser Gly Ser Ala Gly Thr Arg Leu Leu Trp Lys Ser Leu Arg
65 70 75 80

Met Trp Phe Ser Ile Thr Cys Cys Thr Glu Met Gly Gln Gly Lys Ala
85 90 95

Trp Ala Val Ser Leu Asn Arg Glu Trp Gly Gly Gly Thr Gly Gln Pro
100 105 110

Ala Leu Ser Pro
115

<210> 163
<211> 67
<212> PRT
<213> Homo sapien

<400> 163

Met Leu Glu Leu Arg Pro Gly Ser Gln Gly Thr Gln Ala Leu His Lys
1 5 10 15

Ile Val Asp Phe Tyr Pro Glu Asp Asn Asn Ser Leu Gln Thr Phe Pro
20 25 30

Ile Pro Ala Ala Glu Val Asp Arg Leu Lys Val Thr Phe Glu Asp Ala
35 40 45

Thr Asp Phe Phe Gly Arg Val Val Ile Tyr His Leu Arg Val Leu Gly
50 55 60

Glu Lys Val
65

<210> 164
<211> 104
<212> PRT
<213> Homo sapien

<400> 164

Gly Trp Thr Gly Cys Val Arg Ile Ser Gly Ala Gly Arg Ser Arg Ile
1   5   10   15

Leu Gln Ala Leu Ala Arg Lys Pro Glu Asp Pro Pro Leu Pro Arg Thr
            20   25   30

Arg Lys Ser Ser Ser Cys Leu Leu Ser Ser Leu Trp Gln Glu Leu Arg
        35   40   45

Ala Leu Glu Leu Leu Gly Pro Ser Gln Gly Leu Pro Tyr Leu Lys Pro
    50   55   60

Gln Leu Gly Pro Leu Ser Pro Pro Gly Met Arg Pro Arg Ala Pro Leu
65   70   75   80

Thr Arg Arg Pro Arg Ser Leu Thr Leu Ile Phe His Arg Val Gln Glu
                85   90   95

Phe Ile Arg Thr Pro Lys Ser Glu
            100

<210> 165
<211> 82
<212> PRT
<213> Homo sapien

<400> 165

Gln Val Pro His Ala Ser Gly Cys Ile Gly Glu Asp Pro Gln Gly Ile
1   5   10   15

Pro Leu Pro Leu Asp Glu Ala His Pro Thr Gly Gly Cys Thr Asn Pro
            20   25   30

Tyr Gly Lys Ser Lys Phe Phe Ile Glu Glu Met Ile Arg Asp Leu Cys
        35   40   45

Gln Ala Asp Lys Gly Trp Thr Ala Ala Leu Gly Leu Asp Arg Met Cys
    50   55   60

Glu Asp Leu Trp Arg Trp Gln Lys Gln Asn Pro Ser Gly Phe Gly Thr
65   70   75   80

Gln Ala

<210> 166
<211> 360
<212> PRT
<213> Homo sapien

<400> 166

Met Ala Glu Lys Val Leu Val Thr Gly Gly Ala Gly Tyr Ile Gly Ser
1 5 10 15

His Thr Val Leu Glu Leu Leu Glu Ala Gly Tyr Leu Pro Val Val Ile
20 25 30

Asp Asn Phe His Asn Ala Phe Arg Gly Gly Gly Ser Leu Pro Glu Ser
35 40 45

Leu Arg Arg Val Gln Glu Leu Thr Gly Arg Ser Val Glu Phe Glu Glu
50 55 60

Met Asp Ile Leu Asp Gln Gly Ala Leu Gln Arg Leu Phe Lys Lys Tyr
65 70 75 80

Ser Phe Met Ala Val Ile His Phe Ala Gly Leu Lys Ala Val Gly Glu
85 90 95

Ser Val Gln Lys Pro Leu Asp Tyr Tyr Arg Val Asn Leu Thr Gly Thr
100 105 110

Ile Gln Leu Leu Glu Ile Met Lys Ala His Gly Val Lys Asn Leu Val
115 120 125

Phe Ser Ser Ser Ala Thr Val Tyr Gly Asn Pro Gln Tyr Leu Pro Leu
130 135 140

Asp Glu Ala His Pro Thr Gly Gly Cys Thr Asn Pro Tyr Gly Lys Ser
145 150 155 160

Lys Phe Phe Ile Glu Glu Met Ile Arg Asp Leu Cys Gln Ala Asp Lys
165 170 175

Thr Trp Asn Ala Val Leu Leu Arg Tyr Phe Asn Pro Thr Gly Ala His
180 185 190

Ala Ser Gly Cys Ile Gly Glu Asp Pro Gln Gly Ile Pro Asn Asn Leu
195 200 205

Met Pro Tyr Val Ser Gln Val Ala Ile Gly Arg Arg Glu Ala Leu Asn

210 215 220

Val Phe Gly Asn Asp Tyr Asp Thr Glu Asp Gly Thr Gly Val Arg Asp
225 230 235 240

Tyr Ile His Val Val Asp Leu Ala Lys Gly His Ile Ala Ala Leu Arg
245 250 255

Lys Leu Lys Glu Gln Cys Gly Cys Arg Val Gly Arg Glu Gly Arg Ser
260 265 270

Glu Gly Gly Glu Gly Pro Asp Pro Gly Arg Ala Ala Gln Arg Arg Gly
275 280 285

Gln Ser Ser Pro Leu His Lys Pro Cys Ser Pro Trp Ala Arg Ser Thr
290 295 300

Thr Trp Ala Arg Ala Gln Ala Ile Gln Cys Cys Arg Trp Ser Arg Leu
305 310 315 320

Trp Arg Arg Pro Leu Gly Arg Arg Ser Arg Thr Arg Trp Trp His Gly
325 330 335

Gly Lys Val Met Trp Gln Pro Val Thr Pro Thr Pro Ala Trp Pro Lys
340 345 350

Arg Ser Trp Gly Gly Gln Gln Pro
355 360

<210> 167
<211> 376
<212> PRT
<213> Homo sapien

<400> 167

Arg Ala Arg Gly Ser Gly Val Gly Gly Gly Ala Ser Ala Ala Ser Val
1 5 10 15

Gly Arg Gly Asn Pro Ser Arg Thr Leu Gln Ser Ser Val Thr Leu Asp
20 25 30

Lys Glu Val Trp Ile Leu Arg Phe His Leu Phe Gln Leu Gln Gly Ala
35 40 45

Met Ala Glu Lys Val Leu Val Thr Gly Gly Ala Gly Tyr Ile Gly Ser
50 55 60

His Thr Val Leu Glu Leu Leu Glu Ala Gly Tyr Leu Pro Val Val Ile
65 70 75 80

Asp Asn Phe His Asn Ala Phe Arg Gly Gly Gly Ser Leu Pro Glu Ser
85 90 95

Leu Arg Arg Val Gln Glu Leu Thr Gly Arg Ser Val Glu Phe Glu Glu
100 105 110

Met Asp Ile Leu Asp Gln Gly Ala Leu Gln Arg Leu Phe Lys Lys Tyr
115 120 125

Ser Phe Met Ala Val Ile His Phe Ala Gly Leu Lys Ala Val Gly Glu
130 135 140

Ser Val Gln Lys Pro Leu Asp Tyr Tyr Arg Val Asn Leu Thr Gly Thr
145 150 155 160

Ile Gln Leu Leu Glu Ile Met Lys Ala His Gly Val Lys Asn Leu Val
165 170 175

Phe Ser Ser Ser Ala Thr Val Tyr Gly Asn Pro Gln Tyr Leu Pro Leu
180 185 190

Asp Glu Ala His Pro Thr Gly Gly Cys Thr Asn Pro Tyr Gly Lys Ser
195 200 205

Lys Phe Phe Ile Glu Glu Met Ile Arg Asp Leu Cys Gln Ala Asp Lys
210 215 220

Thr Trp Asn Ala Val Leu Leu Arg Tyr Phe Asn Pro Thr Gly Ala His
225 230 235 240

Ala Ser Gly Cys Ile Gly Glu Asp Pro Gln Gly Ile Pro Asn Asn Leu
245 250 255

Met Pro Tyr Val Ser Gln Val Ala Ile Gly Arg Arg Glu Ala Leu Asn
260 265 270

Val Phe Gly Asn Asp Tyr Asp Thr Glu Asp Gly Thr Gly Val Arg Asp
275 280 285

Tyr Ile His Val Val Asp Leu Ala Lys Gly His Ile Ala Ala Leu Arg
290 295 300

Lys Leu Lys Glu Gln Cys Gly Cys Arg Val Gly Arg Glu Gly Arg Ser
305 310 315 320

Glu Gly Gly Glu Gly Pro Asp Pro Gly Arg Ala Ala Gln Arg Arg Gly
325 330 335

Gln Ser Ser Pro Leu His Lys Pro Cys Ser Pro Trp Ala Arg Ser Thr
340 345 350

Thr Trp Ala Arg Ala Gln Ala Ile Gln Cys Cys Arg Trp Ser Arg Leu
355 360 365

Trp Arg Arg Pro Leu Gly Arg Arg
370 375

<210> 168
<211> 466
<212> PRT
<213> Homo sapien

<400> 168

Met Ala Glu Lys Val Leu Val Thr Gly Gly Ala Gly Tyr Ile Gly Ser
1 5 10 15

His Thr Val Leu Glu Leu Leu Glu Ala Gly Tyr Leu Pro Val Val Ile
20 25 30

Asp Asn Phe His Asn Ala Phe Arg Gly Gly Gly Ser Leu Pro Glu Ser
35 40 45

Leu Arg Arg Val Gln Glu Leu Thr Gly Arg Ser Val Glu Phe Glu Glu
50 55 60

Met Asp Ile Leu Asp Gln Gly Ala Leu Gln Arg Leu Phe Lys Lys Tyr
65 70 75 80

Ser Phe Met Ala Val Ile His Phe Ala Gly Leu Lys Ala Val Gly Glu
85 90 95

Ser Val Gln Lys Pro Leu Asp Tyr Tyr Arg Val Asn Leu Thr Gly Thr
100 105 110

Ile Gln Leu Leu Glu Ile Met Lys Ala His Gly Val Lys Asn Leu Val
115 120 125

Phe Ser Ser Ser Ala Thr Val Tyr Gly Asn Pro Gln Tyr Leu Pro Leu
130 135 140

Asp Glu Ala His Pro Thr Gly Gly Cys Thr Asn Pro Tyr Gly Lys Ser
145 150 155 160

Lys Phe Phe Ile Glu Glu Met Ile Arg Asp Leu Cys Gln Ala Asp Lys
165 170 175

Thr Trp Asn Ala Val Leu Leu Arg Tyr Phe Asn Pro Thr Gly Ala His
180 185 190

Ala Ser Gly Cys Ile Gly Glu Asp Pro Gln Gly Ile Pro Asn Asn Leu
195 200 205

Met Pro Tyr Val Ser Gln Val Ala Ile Gly Arg Arg Glu Ala Leu Asn
210 215 220

Val Phe Gly Asn Asp Tyr Asp Thr Glu Asp Gly Thr Gly Val Arg Asp
225 230 235 240

Tyr Ile His Val Val Asp Leu Ala Lys Gly His Ile Ala Ala Leu Arg
245 250 255

Lys Leu Lys Glu Gln Cys Gly Cys Arg Val Gly Arg Glu Gly Arg Ser
260 265 270

Glu Gly Gly Glu Gly Pro Asp Pro Gly Arg Ala Ala Gln Arg Arg Gly
275 280 285

Gln Ser Ser Pro Leu His Lys Pro Cys Ser Pro Trp Ala Arg Ser Thr
290 295 300

Thr Trp Ala Arg Ala Gln Ala Ile Gln Cys Cys Arg Trp Ser Arg Leu
305 310 315 320

Trp Arg Arg Pro Leu Gly Arg Arg Ser Gly Pro Pro Thr Pro Pro Thr
325 330 335

Ser Pro Thr Ser Pro His Pro Ala Leu Ser Asn Arg Ala Ala Leu Ala
340 345 350

Leu Pro Thr His Leu Ser Gly Gly Tyr Leu Ala Leu Pro Ser Leu Leu
355 360 365

Ser Leu Pro Ser Thr Arg Cys Leu Arg Ala Ser Arg Cys Ser Ala Leu
370 375 380

Leu Leu Leu Lys Asp Leu Ala Ser Ser Trp Ala Arg Ala Gly Ser Ala
385 390 395 400

Lys Leu Gln Leu Pro Pro Val Leu Gln Ile Pro Tyr Lys Val Val Ala
405 410 415

Arg Arg Glu Gly Asp Val Ala Ala Cys Tyr Ala Asn Pro Ser Leu Ala
420 425 430

Gln Glu Glu Leu Gly Trp Thr Ala Ala Leu Gly Leu Asp Arg Met Cys
435 440 445

Glu Asp Leu Trp Arg Trp Gln Lys Gln Asn Pro Ser Gly Phe Gly Thr
450 455 460

Gln Ala
465

<210> 169
<211> 328
<212> PRT
<213> Homo sapien

<400> 169

Met Ala Glu Lys Val Leu Val Thr Gly Gly Ala Gly Tyr Ile Gly Ser
1 5 10 15

His Thr Val Leu Glu Leu Leu Glu Ala Gly Tyr Leu Pro Val Val Ile
20 25 30

Asp Asn Phe His Asn Ala Phe Arg Gly Gly Gly Ser Leu Pro Glu Ser
35 40 45

Leu Arg Arg Val Gln Glu Leu Thr Gly Arg Ser Val Glu Phe Glu Glu
50 55 60

Met Asp Ile Leu Asp Gln Gly Ala Leu Gln Arg Leu Phe Lys Lys Tyr
65 70 75 80

Ser Phe Met Ala Val Ile His Phe Ala Gly Leu Lys Ala Val Gly Glu
85 90 95

Ser Val Gln Lys Pro Leu Asp Tyr Tyr Arg Val Asn Leu Thr Gly Thr
100 105 110

Ile Gln Leu Leu Glu Ile Met Lys Ala His Gly Val Lys Asn Leu Val

115 120 125

Phe Ser Ser Ser Ala Thr Val Tyr Gly Asn Pro Gln Tyr Leu Pro Leu
130 135 140

Asp Glu Ala His Pro Thr Gly Gly Cys Thr Asn Pro Tyr Gly Lys Ser
145 150 155 160

Lys Phe Phe Ile Glu Glu Met Ile Arg Asp Leu Cys Gln Ala Asp Lys
165 170 175

Thr Trp Asn Ala Val Leu Leu Arg Tyr Phe Asn Pro Thr Gly Ala His
180 185 190

Ala Ser Gly Cys Ile Gly Glu Asp Pro Gln Gly Ile Pro Asn Asn Leu
195 200 205

Met Pro Tyr Val Ser Gln Val Ala Ile Gly Arg Arg Glu Ala Leu Asn
210 215 220

Val Phe Gly Asn Asp Tyr Asp Thr Glu Asp Gly Thr Gly Val Arg Asp
225 230 235 240

Tyr Ile His Val Val Asp Leu Ala Lys Gly His Ile Ala Ala Leu Arg
245 250 255

Lys Leu Lys Glu Gln Cys Gly Cys Arg Val Gly Arg Glu Gly Arg Ser
260 265 270

Glu Gly Gly Glu Gly Pro Asp Pro Gly Arg Ala Ala Gln Arg Arg Gly
275 280 285

Gln Ser Ser Pro Leu His Lys Pro Cys Ser Pro Trp Ala Arg Ser Thr
290 295 300

Thr Trp Ala Arg Ala Gln Ala Ile Gln Cys Cys Arg Trp Ser Arg Leu
305 310 315 320

Trp Arg Arg Pro Leu Gly Arg Arg
325

<210> 170
<211> 178
<212> PRT
<213> Homo sapien

<400> 170

Met Ala Ser Thr Ser Tyr Asp Tyr Cys Arg Val Pro Met Glu Asp Gly
1   5   10   15

Asp Lys Arg Cys Lys Leu Leu Leu Gly Ile Gly Ile Leu Val Leu Leu
            20   25   30

Ile Ile Val Ile Leu Gly Val Pro Leu Ile Ile Phe Thr Ile Lys Ala
        35   40   45

Asn Ser Glu Ala Cys Arg Asp Gly Leu Arg Ala Val Met Glu Cys Arg
    50   55   60

Asn Val Thr His Leu Leu Gln Gln Glu Leu Thr Glu Ala Gln Lys Gly
65   70   75   80

Phe Gln Asp Val Glu Ala Gln Ala Ala Thr Cys Asn His Thr Val Met
                85   90   95

Ala Leu Met Ala Ser Leu Asp Ala Glu Lys Ala Gln Gly Gln Lys Lys
            100   105   110

Val Glu Glu Leu Glu Gly Glu Ile Thr Thr Leu Asn His Lys Leu Gln
        115   120   125

Asp Ala Ser Ala Glu Val Glu Arg Leu Arg Arg Glu Asn Gln Val Leu
    130   135   140

Ser Val Arg Ile Ala Asp Lys Lys Tyr Tyr Pro Ser Ser Gln Asp Ser
145   150   155   160

Ser Ser Ala Ala Ala Pro Gln Gln His Asn Gln Gln Leu Gly Arg Arg
                165   170   175

Ser Cys

<210> 171
<211> 141
<212> PRT
<213> Homo sapien

<400> 171

Leu Gln Ala Arg Leu Leu Ser Ala Lys Gly Glu Ile Trp Met Ala Ser
1   5   10   15

Thr Ser Tyr Asp Tyr Cys Arg Val Pro Met Glu Asp Gly Asp Lys Arg

20 25 30

Cys Lys Leu Leu Leu Gly Ile Gly Ile Leu Val Leu Leu Ile Ile Val
35 40 45

Ile Leu Gly Val Pro Leu Ile Ile Phe Thr Ile Lys Ala Asn Ser Glu
50 55 60

Ala Cys Arg Asp Gly Leu Arg Ala Val Met Glu Cys Arg Asn Val Thr
65 70 75 80

His Leu Leu Gln Gln Glu Leu Thr Glu Ala Gln Lys Gly Phe Gln Asp
85 90 95

Val Glu Ala Gln Ala Ala Thr Cys Asn His Thr Val Met Ala Leu Met
100 105 110

Ala Ser Leu Asp Ala Glu Lys Ala Gln Gly Gln Lys Lys Val Glu Glu
115 120 125

Leu Glu Val Thr Thr Leu Asn His Lys Leu Gln Asp Ala
130 135 140

<210> 172
<211> 188
<212> PRT
<213> Homo sapien

<400> 172

Met Ala Ser Thr Ser Tyr Asp Tyr Cys Arg Val Pro Met Glu Asp Gly
1 5 10 15

Asp Lys Arg Cys Lys Leu Leu Leu Gly Ile Gly Ile Leu Val Leu Leu
20 25 30

Ile Ile Val Ile Leu Gly Val Pro Leu Ile Ile Phe Thr Ile Lys Ala
35 40 45

Asn Ser Glu Ala Cys Arg Asp Gly Leu Arg Ala Val Met Glu Cys Arg
50 55 60

Asn Val Thr His Leu Leu Gln Gln Glu Leu Thr Glu Ala Gln Lys Gly
65 70 75 80

Phe Gln Asp Val Glu Ala Gln Ala Ala Thr Cys Asn His Thr Val Met
85 90 95

Ala Leu Met Ala Ser Leu Asp Ala Glu Lys Ala Gln Gly Gln Lys Lys
100 105 110

Val Glu Glu Leu Glu Val Thr Thr Leu Asn His Lys Leu Gln Asp Ala
115 120 125

Ser Arg Pro Gly Phe Leu Phe Ser Val Ala Pro Pro Leu Gln Thr Arg
130 135 140

Leu Arg Arg Glu Asn Gln Val Leu Ser Val Arg Ile Ala Asp Lys Lys
145 150 155 160

Tyr Tyr Pro Ser Ser Gln Asp Ser Ser Ser Ala Ala Ala Pro Gln Leu
165 170 175

Leu Ile Val Leu Leu Gly Leu Ser Ala Leu Leu Gln
180 185

<210> 173
<211> 78
<212> PRT
<213> Homo sapien

<400> 173

Met Pro Trp Ile Gly Gly Gly Leu Ile Ala Val Trp Gly Gly Ala Ile
1 5 10 15

Asn Gly Gly Gly Ser Ile Asp Gly Gly Glu Gly Leu Met Asp Gly Trp
20 25 30

Gly Gly Ser Ser Asp Gly Gly Gly Ala Trp Gly Arg Ala Trp Ser Gly
35 40 45

Ala Ser Ala Cys Cys Leu Gln Ser Ala Leu Ser Pro Ser Ser Gly Pro
50 55 60

Leu Gly Thr Ser Trp Lys Val Arg Pro Ala Arg Leu Phe Ala
65 70 75

<210> 174
<211> 116
<212> PRT
<213> Homo sapien

<400> 174

Met Leu Trp Val Trp Phe His Ile Thr Ala Ile Lys Leu Gln Arg Glu
1 5 10 15

Glu Glu Glu Ala Phe Ala Ser Ser Gln Ser Ser Gln Gly Ala Gln Ser
20 25 30

Leu Ile Phe Ser Lys Phe Glu Gly Lys Lys Thr Asn Lys Lys Thr Arg
35 40 45

Lys Val Thr Thr Val Lys Lys Ser Ser Val Arg Leu Pro Gly Ser Asp
50 55 60

Gln Arg Arg Ile Leu Lys Trp Ile Pro Gly Val Cys Leu Glu Thr Ser
65 70 75 80

Trp Pro Ala Ser Pro Ser Ala Ala Ser Thr Ser Ser Met Pro Ser Arg
85 90 95

Ser Pro Arg Thr Ser Trp Arg Gln Gln Met Thr Ser Ser Pro Pro Ser
100 105 110

Ser Thr Leu Phe
115

<210> 175
<211> 360
<212> PRT
<213> Homo sapien

<400> 175

Met Ala Thr Lys Gly Gly Thr Val Lys Ala Ala Ser Gly Phe Asn Ala
1 5 10 15

Met Glu Asp Ala Gln Thr Leu Arg Lys Ala Met Lys Gly Leu Ala Gln
20 25 30

Thr Thr Arg Lys Gln Lys Ile His Gln Thr Phe Met Asn Ser Gln Leu
35 40 45

Leu Glu Arg Gln Gly Thr Asn Leu Lys Asn Gln Asn Lys Val Ser Leu
50 55 60

Leu Lys Leu Leu Gln Glu Thr Gly Thr Asp Glu Asp Ala Ile Ile Ser
65 70 75 80

Val Leu Ala Tyr Arg Asn Thr Ala Gln Arg Gln Glu Ile Arg Thr Ala
85 90 95

Tyr Lys Ser Thr Ile Gly Arg Asp Leu Ile Asp Asp Leu Lys Ser Glu
100 105 110

Leu Ser Gly Asn Phe Glu Gln Val Ile Val Gly Met Met Thr Pro Thr
115 120 125

Val Leu Tyr Asp Val Gln Glu Leu Arg Arg Ala Met Lys Gly Ala Gly
130 135 140

Thr Asp Glu Gly Cys Leu Ile Glu Ile Leu Ala Ser Arg Thr Pro Glu
145 150 155 160

Glu Ile Arg Arg Ile Ser Gln Thr Tyr Gln Gln Gln Tyr Gly Arg Ser
165 170 175

Leu Glu Asp Asp Ile Arg Ser Asp Thr Ser Phe Met Phe Gln Arg Val
180 185 190

Leu Val Ser Leu Ser Ala Gly Gly Arg Asp Glu Gly Asn Tyr Leu Asp
195 200 205

Asp Ala Leu Val Arg Gln Asp Ala Gln Asp Leu Tyr Glu Ala Gly Glu
210 215 220

Lys Lys Trp Gly Thr Asp Glu Val Lys Phe Leu Thr Val Leu Cys Ser
225 230 235 240

Arg Asn Arg Asn His Leu Leu His Val Phe Asp Glu Tyr Lys Arg Ile
245 250 255

Ser Gln Lys Asp Ile Glu Gln Ser Ile Lys Ser Glu Thr Ser Gly Ser
260 265 270

Phe Glu Asp Ala Leu Leu Ala Ile Val Lys Cys Met Arg Asn Lys Ser
275 280 285

Ala Tyr Phe Ala Glu Lys Leu Tyr Lys Ser Met Lys Gly Leu Gly Thr
290 295 300

Asp Asp Asn Thr Leu Ile Arg Val Met Val Ser Arg Ala Glu Ile Asp
305 310 315 320

Met Leu Asp Ile Arg Ala His Phe Lys Arg Leu Tyr Gly Lys Ser Leu
325 330 335

Tyr Ser Phe Ile Lys Gly Asp Thr Ser Gly Asp Tyr Arg Lys Val Leu

340 345 350

Leu Val Leu Cys Gly Gly Asp Asp
355 360

<210> 176
<211> 177
<212> PRT
<213> Homo sapien

<400> 176

Met Tyr Thr Leu Glu Leu Phe Phe Ile Cys Phe Ser His Pro Gln Gly
1 5 10 15

Gly Arg Asp Glu Gly Asn Tyr Leu Asp Asp Ala Leu Val Arg Gln Asp
20 25 30

Ala Gln Asp Leu Tyr Glu Ala Gly Glu Lys Lys Trp Gly Thr Asp Glu
35 40 45

Val Lys Phe Leu Thr Val Leu Cys Ser Arg Asn Arg Asn His Leu Leu
50 55 60

His Val Phe Asp Glu Tyr Lys Arg Ile Ser Gln Lys Asp Ile Glu Gln
65 70 75 80

Ser Ile Lys Ser Glu Thr Ser Gly Ser Phe Glu Asp Ala Leu Leu Ala
85 90 95

Ile Val Lys Cys Met Arg Asn Lys Ser Ala Tyr Phe Ala Glu Lys Leu
100 105 110

Tyr Lys Ser Met Lys Gly Leu Gly Thr Asp Asp Asn Thr Leu Ile Arg
115 120 125

Val Met Val Ser Arg Ala Glu Ile Asp Met Leu Asp Ile Arg Ala His
130 135 140

Phe Lys Arg Leu Tyr Gly Lys Ser Leu Tyr Ser Phe Ile Lys Gly Asp
145 150 155 160

Thr Ser Gly Asp Tyr Arg Lys Val Leu Leu Val Leu Cys Gly Gly Asp
165 170 175

Asp

<210> 177
<211> 380
<212> PRT
<213> Homo sapien

<400> 177

Met Tyr Phe Asp Trp Gly Pro Gly Glu Met Leu Val Cys Glu Thr Ser
1 5 10 15

Phe Asn Lys Lys Glu Lys Ser Glu Met Val Pro Ser Cys Pro Phe Ile
20 25 30

Tyr Ile Ile Arg Lys Asp Val Asp Val Tyr Ser Gln Ile Leu Arg Lys
35 40 45

Leu Phe Asn Glu Ser His Gly Ile Phe Leu Gly Leu Gln Arg Ile Asp
50 55 60

Glu Glu Leu Thr Gly Lys Ser Arg Lys Ser Gln Leu Val Arg Val Ser
65 70 75 80

Lys Asn Tyr Arg Ser Val Ile Arg Ala Cys Met Glu Glu Met His Gln
85 90 95

Val Ala Ile Ala Ala Lys Asp Pro Ala Asn Gly Arg Gln Phe Ser Ser
100 105 110

Gln Val Ser Ile Leu Ser Ala Met Glu Leu Ile Trp Asn Leu Cys Glu
115 120 125

Ile Leu Phe Ile Glu Val Ala Pro Ala Gly Pro Leu Leu Leu His Leu
130 135 140

Leu Asp Trp Val Arg Leu His Val Cys Glu Val Asp Ser Leu Ser Ala
145 150 155 160

Asp Val Leu Gly Ser Glu Asn Pro Ser Lys His Asp Ser Phe Trp Asn
165 170 175

Leu Val Thr Ile Leu Val Leu Gln Gly Arg Leu Asp Glu Ala Arg Gln
180 185 190

Met Leu Ser Lys Glu Ala Asp Ala Ser Pro Ala Ser Ala Gly Ile Cys
195 200 205

Arg Ile Met Gly Asp Leu Met Arg Thr Met Pro Ile Leu Ser Pro Gly

210 215 220

Asn Thr Gln Thr Leu Thr Glu Leu Glu Leu Lys Trp Gln His Trp His
225 230 235 240

Glu Glu Cys Glu Arg Tyr Leu Gln Asp Ser Thr Phe Ala Thr Ser Pro
245 250 255

His Leu Glu Ser Leu Leu Lys Ile Met Leu Gly Asp Glu Ala Ala Leu
260 265 270

Leu Glu Gln Lys Glu Leu Leu Ser Asn Trp Tyr His Phe Leu Val Thr
275 280 285

Arg Leu Leu Tyr Ser Asn Pro Thr Val Lys Pro Ile Asp Leu His Tyr
290 295 300

Tyr Ala Gln Ser Ser Leu Asp Leu Phe Leu Gly Gly Glu Ser Ser Pro
305 310 315 320

Glu Pro Leu Asp Asn Ile Leu Leu Ala Ala Phe Glu Phe Asp Ile His
325 330 335

Gln Val Ile Lys Glu Cys Arg Asn Lys Thr Asp Leu Ser Arg Arg Ser
340 345 350

Leu Leu Asp Ala Gly Ser Ile Lys Gly Glu Ser Ile Leu Leu Phe Pro
355 360 365

Val Ala Glu Glu Lys Glu Lys Tyr His Glu Glu Gly
370 375 380

<210> 178
<211> 394
<212> PRT
<213> Homo sapien

<400> 178

Glu Leu Arg Leu Leu Ser Tyr Phe Arg Leu Val Cys Phe Pro Ser Gly
1 5 10 15

Arg Glu Ala Leu Val Pro Phe Pro Arg Leu Ser Cys His Phe Ser Gly
20 25 30

Gly Arg Ser Val Asn Glu Leu Ile Pro Gly Val Asn Ser Lys Lys Asn
35 40 45

Gln Met Tyr Phe Asp Trp Gly Pro Gly Glu Met Leu Val Cys Glu Thr
50 55 60

Ser Phe Asn Lys Lys Glu Lys Ser Glu Met Val Pro Ser Cys Pro Phe
65 70 75 80

Ile Tyr Ile Ile Arg Lys Asp Val Asp Val Tyr Ser Gln Ile Leu Arg
85 90 95

Lys Leu Phe Asn Glu Ser His Gly Ile Phe Leu Gly Leu Gln Arg Ile
100 105 110

Asp Glu Glu Leu Thr Gly Lys Ser Arg Lys Ser Gln Leu Val Arg Val
115 120 125

Ser Lys Asn Tyr Arg Ser Val Ile Arg Ala Cys Met Glu Glu Met His
130 135 140

Gln Val Ala Ile Ala Ala Lys Asp Pro Ala Asn Gly Arg Gln Phe Ser
145 150 155 160

Ser Gln Val Ser Ile Leu Ser Ala Met Glu Leu Ile Trp Asn Leu Cys
165 170 175

Glu Ile Leu Phe Ile Glu Val Ala Pro Ala Gly Pro Leu Leu Leu His
180 185 190

Leu Leu Asp Trp Val Arg Leu His Val Cys Glu Val Asp Ser Leu Ser
195 200 205

Ala Asp Val Leu Gly Ser Glu Asn Pro Ser Lys His Asp Ser Phe Trp
210 215 220

Asn Leu Val Thr Ile Leu Val Leu Gln Gly Arg Leu Asp Glu Ala Arg
225 230 235 240

Gln Met Leu Ser Lys Glu Ala Asp Ala Ser Pro Ala Ser Ala Gly Ile
245 250 255

Cys Arg Ile Met Gly Asp Leu Met Arg Thr Met Pro Ile Leu Ser Pro
260 265 270

Gly Asn Thr Gln Thr Leu Thr Glu Leu Glu Leu Lys Trp Gln His Trp
275 280 285

His Glu Glu Cys Glu Arg Tyr Leu Gln Asp Ser Thr Phe Ala Thr Ser
290 295 300

Pro His Leu Glu Ser Leu Leu Lys Ile Met Leu Gly Asp Glu Ala Ala
305 310 315 320

Leu Leu Glu Gln Lys Glu Leu Leu Ser Asn Trp Tyr His Phe Leu Val
325 330 335

Thr Arg Leu Leu Tyr Ser Asn Pro Thr Val Lys Pro Ile Asp Leu His
340 345 350

Tyr Tyr Ala Gln Ser Ser Leu Asp Leu Phe Leu Gly Gly Glu Ser Ser
355 360 365

Pro Glu Pro Leu Asp Asn Ile Leu Leu Ala Ala Phe Glu Phe Asp Ile
370 375 380

His Gln Val Ile Lys Glu Cys Ser Phe Leu
385 390

<210> 179
<211> 679
<212> PRT
<213> Homo sapien

<400> 179

Met Tyr Phe Asp Trp Gly Pro Gly Glu Met Leu Val Cys Glu Thr Ser
1 5 10 15

Phe Asn Lys Lys Glu Lys Ser Glu Met Val Pro Ser Cys Pro Phe Ile
20 25 30

Tyr Ile Ile Arg Lys Asp Val Asp Val Tyr Ser Gln Ile Leu Arg Lys
35 40 45

Leu Phe Asn Glu Ser His Gly Ile Phe Leu Gly Leu Gln Arg Ile Asp
50 55 60

Glu Glu Leu Thr Gly Lys Ser Arg Lys Ser Gln Leu Val Arg Val Ser
65 70 75 80

Lys Asn Tyr Arg Ser Val Ile Arg Ala Cys Met Glu Glu Met His Gln
85 90 95

Val Ala Ile Ala Ala Lys Asp Pro Ala Asn Gly Arg Gln Phe Ser Ser
100 105 110

Gln Val Ser Ile Leu Ser Ala Met Glu Leu Ile Trp Asn Leu Cys Glu
115 120 125

Ile Leu Phe Ile Glu Val Ala Pro Ala Gly Pro Leu Leu Leu His Leu
130 135 140

Leu Asp Trp Val Arg Leu His Val Cys Glu Val Asp Ser Leu Ser Ala
145 150 155 160

Asp Val Leu Gly Ser Glu Asn Pro Ser Lys His Asp Ser Phe Trp Asn
165 170 175

Leu Val Thr Ile Leu Val Leu Gln Gly Arg Leu Asp Glu Ala Arg Gln
180 185 190

Met Leu Ser Lys Glu Ala Asp Ala Ser Pro Ala Ser Ala Gly Ile Cys
195 200 205

Arg Ile Met Gly Asp Leu Met Arg Thr Met Pro Ile Leu Ser Pro Gly
210 215 220

Asn Thr Gln Thr Leu Thr Glu Leu Glu Leu Lys Trp Gln His Trp His
225 230 235 240

Glu Glu Cys Glu Arg Tyr Leu Gln Asp Ser Thr Phe Ala Thr Ser Pro
245 250 255

His Leu Glu Ser Leu Leu Lys Ile Met Leu Gly Asp Glu Ala Ala Leu
260 265 270

Leu Glu Gln Lys Glu Leu Leu Ser Asn Trp Tyr His Phe Leu Val Thr
275 280 285

Arg Leu Leu Tyr Ser Asn Pro Thr Val Lys Pro Ile Asp Leu His Tyr
290 295 300

Tyr Ala Gln Ser Ser Leu Asp Leu Phe Leu Gly Gly Glu Ser Ser Pro
305 310 315 320

Glu Pro Leu Asp Asn Ile Leu Leu Ala Ala Phe Glu Phe Asp Ile His
325 330 335

Gln Val Ile Lys Glu Cys Ser Phe Leu Leu Lys Thr Gly Gln Phe Leu
340 345 350

Ala Val Trp Gln Glu Glu Thr Ala Gly Val His Phe Thr Gly Ser Trp
355 360 365

Ala Arg Cys Arg Gln Phe Pro Gly Ala Leu Gln Val Leu Gln Lys Tyr
370 375 380

Arg Ala Lys Ser Ile Ala Leu Ser Asn Trp Trp Phe Val Ala His Leu
385 390 395 400

Thr Asp Leu Leu Asp His Cys Lys Leu Leu Gln Ser His Asn Leu Tyr
405 410 415

Phe Gly Ser Asn Met Arg Glu Phe Leu Leu Leu Glu Tyr Ala Ser Gly
420 425 430

Leu Phe Ala His Pro Ser Leu Trp Gln Leu Gly Val Asp Tyr Phe Asp
435 440 445

Tyr Cys Pro Glu Leu Gly Arg Val Ser Leu Glu Leu His Ile Glu Arg
450 455 460

Ile Pro Leu Asn Thr Glu Gln Lys Ala Leu Lys Val Leu Arg Ile Cys
465 470 475 480

Glu Gln Arg Gln Met Thr Glu Gln Val Arg Ser Ile Cys Lys Ile Leu
485 490 495

Ala Met Lys Ala Val Arg Asn Asn Arg Leu Gly Ser Ala Leu Ser Trp
500 505 510

Ser Ile Arg Ala Lys Asp Ala Ala Phe Ala Thr Leu Val Ser Asp Arg
515 520 525

Phe Leu Arg Asp Tyr Cys Glu Arg Gly Cys Phe Ser Asp Leu Asp Leu
530 535 540

Ile Asp Asn Leu Gly Pro Ala Met Met Leu Ser Asp Arg Leu Thr Phe
545 550 555 560

Leu Gly Lys Tyr Arg Glu Phe His Arg Met Tyr Gly Glu Lys Arg Phe
565 570 575

Ala Asp Ala Ala Ser Leu Leu Leu Ser Leu Met Thr Ser Arg Ile Ala
580 585 590

Pro Arg Ser Phe Trp Met Thr Leu Leu Thr Asp Ala Leu Pro Leu Leu
595 600 605

Glu Gln Lys Gln Val Ile Phe Ser Ala Glu Gln Thr Tyr Glu Leu Met
610 615 620

Arg Cys Leu Glu Asp Leu Thr Ser Arg Arg Pro Val His Gly Glu Ser
625 630 635 640

Asp Thr Glu Gln Leu Gln Asp Asp Asp Ile Glu Thr Thr Lys Val Glu
645 650 655

Met Leu Arg Leu Ser Leu Ala Arg Asn Leu Ala Arg Ala Ile Ile Arg
660 665 670

Glu Gly Ser Leu Glu Gly Ser
675

<210> 180
<211> 72
<212> PRT
<213> Homo sapien

<220>
<221> MISC_FEATURE
<222> (45)..(45)
<223> X=any amino acid

<400> 180

Arg Cys Asn Thr Pro Thr Ser Ser Gln Ile Lys Phe Gln His Ile Leu
1 5 10 15

Tyr Ala Ser Val Thr Lys Gln Pro His Asn Leu Val Phe Ile Val Asp
20 25 30

Leu Tyr Arg Met Lys Glu Glu Asn Pro Leu Trp His Xaa Asn Glu Ser
35 40 45

Phe Trp Trp Gly Gln Leu Thr Arg Pro Arg Gly Gln Arg Ser Arg Ser
50 55 60

Glu Ser Arg Pro Thr Arg Pro Trp
65 70

<210> 181
<211> 77
<212> PRT
<213> Homo sapien

<400> 181

Arg Cys Asn Thr Pro Thr Ser Ser Gln Ile Lys Phe Gln His Ile Leu
1 5 10 15

Tyr Ala Ser Val Thr Lys Gln Pro His Asn Leu Val Phe Ile Val Asp
20 25 30

Leu Tyr Arg Met Lys Glu Glu Asn Pro Leu Trp His Ala Asn Glu Ile
35 40 45

Phe Leu Val Gly Thr Ala Asp Glu Ala Thr Arg Ala Glu Ile Gln Ile
50 55 60

Arg Ile Glu Ala Asn Glu Ala Leu Val Lys Ala Leu Glu
65 70 75

<210> 182
<211> 174
<212> PRT
<213> Homo sapien

<400> 182

Ser Lys Cys His Val Tyr Thr Leu Asn Ile Leu Lys Ile Cys Phe Phe
1 5 10 15

Tyr Phe Arg Lys Phe Ile Glu Met Gly Phe Ile Asp Glu Lys Arg Ile
20 25 30

Ala Ile Trp Gly Trp Ser Tyr Gly Gly Tyr Val Ser Ser Leu Ala Leu
35 40 45

Ala Ser Gly Thr Gly Leu Phe Lys Cys Gly Ile Ala Val Ala Pro Val
50 55 60

Ser Ser Trp Glu Tyr Tyr Ala Ser Val Tyr Thr Glu Arg Phe Met Gly
65 70 75 80

Leu Pro Thr Lys Asp Asp Asn Leu Glu His Tyr Lys Asn Ser Thr Val
85 90 95

Met Ala Arg Ala Glu Tyr Phe Arg Asn Val Asp Tyr Leu Leu Ile His
100 105 110

Gly Thr Ala Asp Asp Asn Val His Phe Gln Asn Ser Ala Gln Ile Ala
115 120 125

Lys Ala Leu Val Asn Ala Gln Val Asp Phe Gln Ala Met Trp Tyr Ser
130 135 140

Asp Gln Asn His Gly Leu Ser Gly Leu Ser Thr Asn His Leu Tyr Thr
145 150 155 160

His Met Thr His Phe Leu Lys Gln Cys Phe Ser Leu Ser Asp
165 170

<210> 183
<211> 36
<212> PRT
<213> Homo sapien

<400> 183

Met Gln Glu Arg Asn Gly Cys Cys Glu Ile Pro Leu Arg Asn Tyr Ile
1 5 10 15

Ile Gln Val Met Lys Ile Thr Gln Phe Tyr Phe Gln Arg Arg Thr Asp
20 25 30

Glu Lys Gly Leu
35

<210> 184
<211> 215
<212> PRT
<213> Homo sapien

<220>
<221> MISC_FEATURE
<222> (207)..(207)
<223> X=any amino acid

<220>
<221> MISC_FEATURE
<222> (211)..(211)
<223> X=any amino acid

<400> 184

Met Leu Pro Ala Val Gly Ser Ala Asp Glu Glu Glu Asp Pro Ala Glu
1 5 10 15

Glu Asp Cys Pro Glu Leu Val Pro Ile Glu Thr Thr Gln Ser Glu Glu
20 25 30

Glu Glu Lys Ser Gly Leu Gly Ala Lys Ile Pro Val Thr Ile Ile Thr
35 40 45

Gly Tyr Leu Gly Ala Gly Lys Thr Thr Leu Leu Asn Tyr Ile Leu Thr
50 55 60

Glu Gln His Ser Lys Arg Val Ala Val Ile Leu Asn Glu Phe Gly Glu
65 70 75 80

Gly Ser Ala Leu Glu Lys Ser Leu Ala Val Ser Gln Gly Gly Glu Leu
85 90 95

Tyr Glu Glu Trp Leu Glu Leu Arg Asn Gly Cys Leu Cys Cys Ser Val
100 105 110

Lys Asp Ser Gly Leu Arg Ala Ile Glu Asn Leu Met Gln Lys Lys Gly
115 120 125

Lys Phe Asp Tyr Ile Leu Leu Glu Thr Thr Gly Leu Ala Asp Pro Gly
130 135 140

Ala Val Ala Ser Met Phe Trp Val Asp Ala Glu Leu Gly Ser Asp Ile
145 150 155 160

Tyr Leu Asp Gly Ile Ile Thr Ile Val Asp Ser Lys Tyr Gly Leu Lys
165 170 175

His Leu Thr Glu Glu Lys Pro Asp Gly Leu Ile Asn Glu Ala Thr Arg
180 185 190

Gln Val Ala Leu Ala Glu Ile Gly Pro Pro Pro Asn Phe Phe Xaa Pro
195 200 205

Phe Ser Xaa Lys Phe Phe Phe
210 215

<210> 185
<211> 133
<212> PRT
<213> Homo sapien

<400> 185

Ile Leu Cys Ile Lys Phe Phe Lys Ser Gln Ser Phe Phe Phe Leu Ile
1 5 10 15

Asn Trp Met Tyr Phe Thr Glu Phe Pro Thr Ala His Val Ser Phe Leu
20 25 30

Pro Phe Arg Val Asp Leu Ser Asn Val Leu Asp Leu His Ala Phe Asp
35 40 45

Ser Leu Ser Gly Ile Ser Leu Gln Lys Lys Leu Gln His Val Pro Gly
50 55 60

Thr Gln Pro His Leu Asp Gln Ser Ile Val Thr Ile Thr Phe Asp Val
65 70 75 80

Pro Gly Asn Ala Lys Glu Glu His Leu Asn Met Phe Ile Gln Asn Leu
85 90 95

Leu Trp Glu Lys Asn Val Arg Asn Lys Asp Asn His Cys Met Glu Val
100 105 110

Ile Arg Leu Lys Val Gln Phe Thr Val Ala Asp Phe Trp Thr Lys Ser
115 120 125

Phe Ser Trp Leu Leu
130

<210> 186
<211> 953
<212> PRT
<213> Homo sapien

<400> 186

Met Ser His Arg Gln Val His Asp Asp Leu Asn Lys Leu Leu Lys Ile
1 5 10 15

Met Leu Ile Asn Ser Phe Gly Ser Val Ile Ile Phe Val Phe Ile Asn
20 25 30

Ile Leu Ser Gln Phe Ser Ser Phe Ile Phe Ile Ser Glu Ile Ser Met
35 40 45

Ser Trp Asn Lys Ser Cys Val Leu Ile Ser Leu Leu Cys Asn Asn Leu
50 55 60

Val Cys Leu Thr Phe Leu Thr Phe Ile Ser Asn Ile Cys Phe Ile Lys
65 70 75 80

Asn Asn Lys His Ala Val Ile Asp Phe Ser Tyr Phe Lys Trp Met Ser
85 90 95

Glu Gln Val Thr Lys Ile Phe Cys Glu Phe Phe Ser Val Trp Cys Leu
100 105 110

Pro Met His Leu Arg Ile Trp Gly Leu Ser Glu Ile Val Leu Pro Cys
115 120 125

Tyr Gly Thr Glu Val Gly Leu Glu Ser Phe Ser Met Lys Ile Arg Cys
130 135 140

Pro Glu Tyr Glu Phe Leu Leu Leu Gly Pro Glu Ser Tyr Ile Lys Tyr
145 150 155 160

Ser Leu Lys Phe Leu Glu Ala Thr Ala Pro Ser Leu Ser Ser Val Ile
165 170 175

Phe Trp Ala Tyr Val Lys Ile Ile Thr Gln Ser Pro Val Phe Ile Asn
180 185 190

Cys Phe Phe Ile Phe Lys Pro Asn Leu Met Leu Ile Val Ile Cys Tyr
195 200 205

Leu Phe Ser Pro Asp Leu Asn His Trp Ile Gln Leu Asn Glu Phe Glu
210 215 220

Leu Ser Leu Asn Asn Ser Lys Arg Asn Asn Val Tyr Ser Asp Gly Gly
225 230 235 240

Asn Phe Leu Ser Thr Cys Ser Pro Ile Leu Asn Glu Val Lys Ser Asn
245 250 255

His Val Thr Ile Arg Val Leu Glu Lys Leu Asn Ile Leu Tyr Ile Gly
260 265 270

Tyr Leu Thr Pro His Phe Tyr Ile Thr Cys Tyr Ile Lys Gly Gly Gly
275 280 285

Ile Lys Glu Ile Gln Lys Leu Gln Arg Tyr Leu Glu Cys Thr Tyr Leu
290 295 300

Leu Ile Leu Phe Val Ile Ser Leu Phe His Leu Leu Ser Asn Lys Leu
305 310 315 320

Leu Glu Lys Phe Leu Phe Phe Ser Cys Phe Phe Ser Tyr Lys Asn Val
325 330 335

Phe Glu Lys Leu Ile Asn Phe Arg Ile Glu Lys Ile Ile Glu Ser Leu
340 345 350

Lys Lys Thr Tyr Phe Ile Glu Val Ile Thr Lys Ile Ile Phe Asn Leu
355 360 365

Asp Ser Thr Val Ile Gln Ile Leu His His Leu Pro Thr Ser Met Asn
370 375 380

Phe Met Tyr Lys Phe Phe Lys Ser Gln Ser Phe Phe Phe Leu Ile Asn
385 390 395 400

Trp Met Tyr Phe Thr Glu Phe Pro Thr Ala His Val Ser Phe Leu Pro
405 410 415

Phe Arg Val Asp Leu Ser Asn Val Leu Asp Leu His Ala Phe Asp Ser
420 425 430

Leu Ser Gly Ile Ser Leu Gln Lys Lys Leu Gln His Val Pro Gly Thr
435 440 445

Gln Pro His Leu Asp Gln Ser Ile Val Thr Ile Thr Phe Asp Val Pro
450 455 460

Gly Asn Ala Lys Glu Glu His Leu Asn Met Phe Ile Gln Asn Leu Leu
465 470 475 480

Trp Glu Lys Asn Val Arg Asn Lys Asp Asn His Cys Met Glu Val Ile
485 490 495

Arg Leu Lys Val Gln Phe Thr Val Ala Asp Phe Trp Thr Lys Ser Phe
500 505 510

Ser Trp Leu Leu Glu Lys Leu Tyr Leu Val Leu Asn Arg Asn Thr Gly
515 520 525

Phe Ser Thr Asn His Leu Cys Leu Leu Ser Phe Phe Phe Ile Ile Phe
530 535 540

Met Thr Glu Lys Glu Leu Trp Lys Ser Leu His Lys Ala Gly Phe Ile
545 550 555 560

Cys Thr Thr Phe Phe Arg Val Ala Ala Arg Thr Asn Leu Cys Ala Leu
565 570 575

Lys Cys Tyr Leu Leu Leu Ser Val Pro Lys Tyr Arg Glu Ile Met Leu
580 585 590

Gln Ile Ser Leu Leu Leu Asn Ile Met Leu Pro Asp Ala Phe Glu Gln
595 600 605

Thr Leu Asn Ile Cys Cys Thr Leu Asn Lys Val Gln Arg Thr Arg Arg
610 615 620

Ile Leu Val Leu Tyr Leu Glu Thr His Ser His Tyr Leu Ile Phe Gly
625 630 635 640

Tyr Leu Ser His Glu Arg Tyr Phe Phe Tyr Gly Ser Ser Asp Ser Gln
645 650 655

Ser Val Cys Leu Thr Ser Gln Leu Ser Val Tyr Ser Cys Val Phe Thr
660 665 670

Ser Val His Lys Val Phe Gly Glu Ile Lys Asn Ile Ile Ser Asn Glu
675 680 685

Ile Asn Phe Ile Pro Ile Gly Ala Ser Leu Ser Asp Asn Ser Phe Leu
690 695 700

Ile Ser Ala Asn Gln Tyr Thr Met Ser Ser Tyr Ser Asp Lys Tyr Asn
705 710 715 720

Ser Phe Ser Leu Phe Gln His Cys Ser Leu Ile Ala Thr His Phe Tyr
725 730 735

Asn Lys Leu Phe Asn Ile Thr Asn Ser Phe Asn Phe Ser Thr Phe Pro
740 745 750

Thr Lys Thr Val Lys His Tyr Ile Lys Ser Leu Ser Ile Gly Tyr Asp
755 760 765

Thr Tyr Phe Ile Ile Leu Phe Gln Val Leu Val Val Ile Asn Asn Thr
770 775 780

Glu Lys Pro Ser Ile Ile Tyr Val Leu Thr Leu Ser Leu Glu Lys Gly
785 790 795 800

Ile Val Gln Lys Lys Ile Asn Thr Gln Lys Pro Phe Leu Lys Ile Lys
805 810 815

Asn Ile Lys Lys Leu Leu Val Ile His Lys Tyr Leu Glu Leu Ser Asn
820 825 830

Phe Leu Ser Phe Lys Ser Leu Tyr Phe Leu Ser Glu Tyr Gln Tyr Ile

835 840 845

Asn Pro Leu Thr Leu Met Leu Ile Ser Ala Phe Lys Phe Glu Leu Arg
850 855 860

Leu Ile Asn Val Gln Ser Ile Leu Leu Gly Ala Gly Leu Val Ser Ile
865 870 875 880

Lys Asp Lys Ser Gln Gln Val Ile Val Gln Gly Val His Glu Leu Tyr
885 890 895

Asp Leu Glu Glu Thr Pro Val Ser Trp Lys Asp Asp Thr Glu Arg Thr
900 905 910

Asn Arg Leu Val Leu Ile Gly Arg Asn Leu Asp Lys Asp Ile Leu Lys
915 920 925

Gln Leu Phe Ile Ala Thr Val Thr Glu Thr Glu Lys Gln Trp Thr Thr
930 935 940

His Phe Lys Glu Asp Gln Val Cys Thr
945 950

<210> 187
<211> 194
<212> PRT
<213> Homo sapien

<400> 187

Ile Leu Cys Ile Lys Phe Phe Lys Ser Gln Ser Phe Phe Phe Leu Ile
1 5 10 15

Asn Trp Met Tyr Phe Thr Glu Phe Pro Thr Ala His Val Ser Phe Leu
20 25 30

Pro Phe Arg Val Asp Leu Ser Asn Val Leu Asp Leu His Ala Phe Asp
35 40 45

Ser Leu Ser Gly Ile Ser Leu Gln Lys Lys Leu Gln His Val Pro Gly
50 55 60

Thr Gln Pro His Leu Asp Gln Ser Ile Val Thr Ile Thr Phe Asp Val
65 70 75 80

Pro Gly Asn Ala Lys Glu Glu His Leu Asn Met Phe Ile Gln Asn Leu
85 90 95

Leu Trp Glu Lys Asn Val Arg Asn Lys Asp Asn His Cys Met Glu Val
100 105 110

Ile Arg Leu Lys Gly Leu Val Ser Ile Lys Asp Lys Ser Gln Gln Val
115 120 125

Ile Val Gln Gly Val His Glu Leu Tyr Asp Leu Glu Glu Thr Pro Val
130 135 140

Ser Trp Lys Asp Asp Thr Glu Arg Thr Asn Arg Leu Val Leu Ile Gly
145 150 155 160

Arg Asn Leu Asp Lys Asp Ile Leu Lys Gln Leu Phe Ile Ala Thr Val
165 170 175

Thr Glu Thr Glu Lys Gln Trp Thr Thr His Phe Lys Glu Asp Gln Val
180 185 190

Cys Thr

<210> 188
<211> 728
<212> PRT
<213> Homo sapien

<400> 188

Met Arg Leu Ser Asn Arg Gln Pro Gly Ala Leu Arg Leu Thr Ala Gly
1 5 10 15

Ser Leu Val Pro Leu Ser Leu Tyr Leu Arg Asn Ser Phe Phe Gly Ser
20 25 30

Thr Ala Glu Ala Leu Gly Glu Trp Leu Cys Leu Leu Trp Gln Arg Leu
35 40 45

Glu Val Leu Thr Asp Cys His Lys Tyr Tyr Ala Val Thr Ala Ala Ala
50 55 60

Ala Tyr Met His Val Asn Ser Trp Gly Ile Asn Leu Val Cys Ile Leu
65 70 75 80

Arg Ser His Ser Ser Ala Gly Arg Gly Ser Arg Arg Met Pro Phe Ser
85 90 95

Val Ser Pro Leu Gln Pro Tyr Thr Lys Cys Ala Pro Cys Val Ser Asn

100 105 110

Ser Ile Val Glu Val Ser Asp Asn Leu Thr Tyr Thr Met Ser His Ser
115 120 125

Ser Val Ser Val Leu Phe Leu Leu Val Phe Tyr Asn Ser Phe Leu Leu
130 135 140

Asn Phe Ser Pro Leu Tyr Lys Met Ser His Arg Gln Val His Asp Thr
145 150 155 160

Tyr Asn Lys Leu Leu Lys Ile Met Leu Ile Asn Ser Phe Gly Ser Val
165 170 175

Ile Ile Phe Val Phe Ile Asn Ile Leu Ser Gln Phe Ser Ser Phe Ile
180 185 190

Phe Ile Ser Glu Ile Ser Met Ser Trp Asn Lys Ser Cys Val Leu Ile
195 200 205

Ser Leu Leu Cys Asn Asn Leu Val Cys Leu Thr Phe Leu Thr Phe Ile
210 215 220

Ser Asn Ile Cys Phe Ile Ile Glu Gln Lys His Ala Val Ile Asp Phe
225 230 235 240

Ser Tyr Phe Lys Trp Met Ser Glu Gln Val Thr Lys Ile Phe Cys Glu
245 250 255

Phe Phe Ser Val Trp Cys Leu Pro Met His Leu Arg Ile Gln Gly Leu
260 265 270

Ser Glu Ile Val Leu Pro Cys Tyr Gly Thr Glu Val Gly Leu Glu Ser
275 280 285

Phe Ser Met Lys Ile Arg Cys Pro Glu Tyr Glu Phe Leu Leu Leu Gly
290 295 300

Pro Glu Ser Tyr Ile Lys Tyr Ser Leu Lys Phe Leu Glu Ala Thr Ala
305 310 315 320

Pro Ser Leu Ser Ser Val Ile Phe Trp Ala Tyr Val Lys Ile Ile Thr
325 330 335

Gln Ser Pro Val Phe Ile Asn Cys Phe Phe Ile Phe Lys Pro Asn Leu
340 345 350

Met Leu Ile Val Ile Cys Tyr Leu Phe Ser Pro Asp Leu Asn His Trp
355 360 365

Ile Gln Leu Asn Glu Phe Glu Leu Ser Leu Asn Asn Ser Lys Arg Asn
370 375 380

Asn Val Tyr Ser Asp Gly Gly Asn Phe Leu Ser Thr Cys Ser Pro Ile
385 390 395 400

Leu Asn Glu Val Lys Ser Asn His Val Thr Ile Arg Val Leu Glu Lys
405 410 415

Leu Asn Ile Leu Tyr Ile Gly Tyr Leu Thr Pro His Phe Tyr Ile Thr
420 425 430

Cys Tyr Ile Lys Gly Gly Gly Ile Lys Glu Ile Gln Lys Leu Gln Arg
435 440 445

Tyr Leu Glu Cys Thr Tyr Leu Leu Ile Leu Phe Val Ile Ser Leu Phe
450 455 460

His Leu Leu Ser Asn Lys Leu Leu Glu Lys Phe Leu Phe Phe Ser Cys
465 470 475 480

Phe Phe Ser Tyr Lys Asn Val Phe Glu Lys Leu Ile Asn Phe Arg Ile
485 490 495

Glu Lys Ile Ile Glu Ser Leu Lys Lys Thr Tyr Phe Ile Glu Val Ile
500 505 510

Thr Lys Ile Ile Phe Asn Leu Asp Ser Thr Val Ile Gln Ile Leu His
515 520 525

His Leu Pro Thr Ser Met Asn Phe Met Tyr Lys Ile Phe Lys Ser Gln
530 535 540

Ser Phe Phe Phe Leu Ile Asn Trp Met Tyr Phe Thr Glu Phe Pro Thr
545 550 555 560

Ala His Val Ser Phe Leu Pro Phe Arg Val Asp Leu Ser Asn Val Leu
565 570 575

Asp Leu His Ala Phe Asp Ser Leu Ser Gly Ile Ser Leu Gln Lys Lys
580 585 590

Leu Gln His Val Pro Gly Thr Gln Pro His Leu Asp Gln Ser Ile Val
595 600 605

Thr Ile Thr Phe Asp Val Pro Gly Asn Ala Lys Glu Glu His Leu Asn
610 615 620

Met Phe Ile Gln Asn Leu Leu Trp Glu Lys Asn Val Arg Asn Lys Asp
625 630 635 640

Asn His Cys Met Glu Val Ile Arg Leu Lys Gly Leu Val Ser Ile Lys
645 650 655

Asp Lys Ser Gln Gln Val Ile Val Gln Gly Val His Glu Leu Tyr Asp
660 665 670

Leu Glu Glu Thr Pro Val Ser Trp Lys Asp Asp Thr Glu Arg Thr Asn
675 680 685

Arg Leu Val Leu Ile Gly Arg Asn Leu Asp Lys Asp Ile Leu Lys Gln
690 695 700

Leu Phe Ile Ala Thr Val Thr Glu Thr Glu Lys Gln Trp Thr Thr His
705 710 715 720

Phe Lys Glu Asp Gln Val Cys Thr
725

<210> 189
<211> 312
<212> PRT
<213> Homo sapien

<400> 189

Met Ala Glu Ile Ser Asp Leu Asp Arg Gln Ile Glu Gln Leu Arg Arg
1 5 10 15

Cys Glu Leu Ile Lys Glu Ser Glu Val Lys Ala Leu Cys Ala Lys Ala
20 25 30

Arg Glu Ile Leu Val Glu Glu Ser Asn Val Gln Arg Val Asp Ser Pro
35 40 45

Val Thr Val Cys Gly Asp Ile His Gly Gln Phe Tyr Asp Leu Lys Glu
50 55 60

Leu Phe Arg Val Gly Gly Asp Val Pro Glu Thr Asn Tyr Leu Phe Met

```
65                  70                  75                  80

Gly Asp Phe Val Asp Arg Gly Phe Tyr Ser Val Glu Thr Phe Leu Leu
                85                  90                  95

Leu Leu Ala Leu Lys Val Arg Tyr Pro Asp Arg Ile Thr Leu Ile Arg
            100                 105                 110

Gly Asn His Glu Ser Arg Gln Ile Thr Gln Val Tyr Gly Phe Tyr Asp
        115                 120                 125

Glu Cys Leu Arg Lys Tyr Gly Ser Val Thr Val Trp Arg Tyr Cys Thr
    130                 135                 140

Glu Ile Phe Asp Tyr Leu Ser Leu Ser Ala Ile Ile Asp Gly Lys Ile
145                 150                 155                 160

Phe Cys Val His Gly Gly Leu Ser Pro Ser Ile Gln Thr Leu Asp Gln
                165                 170                 175

Ile Arg Thr Ile Asp Arg Lys Gln Glu Val Pro His Asp Gly Pro Met
            180                 185                 190

Cys Asp Leu Leu Trp Ser Asp Pro Glu Asp Thr Thr Gly Trp Gly Val
        195                 200                 205

Ser Pro Arg Gly Ala Gly Tyr Leu Phe Gly Ser Asp Val Val Ala Gln
    210                 215                 220

Phe Asn Ala Ala Asn Asp Ile Asp Met Ile Cys Arg Ala His Gln Leu
225                 230                 235                 240

Val Met Glu Gly Tyr Lys Trp His Phe Asn Glu Thr Val Leu Thr Val
                245                 250                 255

Trp Ser Ala Pro Asn Tyr Cys Tyr Arg Cys Gly Asn Val Ala Ala Ile
            260                 265                 270

Leu Glu Leu Asp Glu His Leu Gln Lys Asp Phe Ile Ile Phe Glu Ala
        275                 280                 285

Ala Pro Gln Glu Thr Arg Gly Asn Pro Ala Arg Pro Leu Pro Pro Pro
    290                 295                 300

Thr Leu Leu Ala Leu Ala Pro Leu
305                 310
```

<210> 190
<211> 182
<212> PRT
<213> Homo sapien

<400> 190

Met Gln Pro Leu Leu His Ser His Ser Gly Pro Pro Cys Asp Asn Thr
1   5   10   15

Gly Cys Pro Ser Val Ser Gly Ser Ala Pro Phe Thr Leu Met Cys Cys
            20   25   30

Leu Asp Gly Asp Cys Met Ile Thr Val Ile Met Arg Gly Pro Gln Ala
        35   40   45

Leu Gly Val Leu Ser Pro Leu Glu Leu Ile Cys Pro Tyr Ile Cys Cys
    50   55   60

Pro Gly Pro Arg His Pro Thr Asp His Ile Gln Ala Pro Cys Ser Gly
65   70   75   80

Pro Thr Gly Leu Trp Trp Thr Trp Gly Gly Ala Arg Leu Leu Thr Leu
                85   90   95

Lys Gly Gln Arg Trp Gln Pro Glu Lys Pro Glu Asp Ile Pro Leu His
            100   105   110

Pro Ser Leu Ser Ala Ser Asp Thr Thr Gly Trp Gly Val Ser Pro Arg
        115   120   125

Gly Ala Gly Tyr Leu Phe Gly Ser Asp Val Val Ala Gln Phe Asn Ala
    130   135   140

Ala Asn Asp Ile Asp Met Ile Cys Arg Ala His Gln Leu Val Met Glu
145   150   155   160

Gly Tyr Lys Trp His Phe Asn Glu Thr Val Leu Thr Val Trp Ser Ala
                165   170   175

Pro Asn Tyr Cys Tyr Arg
            180

<210> 191
<211> 293
<212> PRT
<213> Homo sapien

<400> 191

Val Pro Ser Gln Ala Leu Gly Ser Gly Ser Arg Arg His Arg Cys Pro
1 5 10 15

Gly Arg Arg Ala Ser Cys Leu Pro Pro Arg Pro Pro Arg Cys Trp Pro
20 25 30

Pro Gly Arg Val Ala Ala Met Leu Leu Pro Trp Ala Thr Ser Ala Pro
35 40 45

Gly Leu Ala Trp Gly Pro Leu Val Leu Gly Leu Phe Gly Leu Leu Ala
50 55 60

Ala Ser Gln Pro Gln Ala Val Pro Pro Tyr Ala Ser Glu Asn Gln Thr
65 70 75 80

Cys Arg Asp Gln Glu Lys Glu Tyr Tyr Glu Pro Gln His Arg Ile Cys
85 90 95

Cys Ser Arg Cys Pro Pro Gly Thr Tyr Val Ser Ala Lys Cys Ser Arg
100 105 110

Ile Arg Asp Thr Val Cys Ala Thr Cys Ala Glu Asn Ser Tyr Asn Glu
115 120 125

His Trp Asn Tyr Leu Thr Ile Cys Gln Leu Cys Arg Pro Cys Asp Pro
130 135 140

Val Met Gly Leu Glu Glu Ile Ala Pro Cys Thr Ser Lys Arg Lys Thr
145 150 155 160

Gln Cys Arg Cys Gln Pro Gly Met Phe Cys Ala Ala Trp Ala Leu Glu
165 170 175

Cys Thr His Cys Glu Leu Leu Ser Asp Cys Pro Pro Gly Thr Glu Ala
180 185 190

Glu Leu Lys Asp Glu Val Gly Lys Gly Asn Asn His Cys Val Pro Cys
195 200 205

Lys Ala Gly His Phe Gln Asn Thr Ser Ser Pro Ser Ala Arg Cys Gln
210 215 220

Pro His Thr Arg Cys Glu Asn Gln Gly Leu Val Glu Ala Ala Pro Gly
225 230 235 240

Thr Ala Gln Ser Asp Thr Thr Cys Lys Asn Pro Leu Glu Pro Leu Pro
245 250 255

Pro Glu Met Ser Glu Pro Ala Leu Ser Lys Gly Val Glu Asn Leu Gln
260 265 270

Ala Leu Leu Tyr Gln Ala Ala Thr Gly Ser Ser Glu Ala Ser Phe Pro
275 280 285

Thr Leu Ser Pro Leu
290

<210> 192
<211> 635
<212> PRT
<213> Homo sapien

<400> 192

Met Leu Leu Pro Trp Ala Thr Ser Ala Pro Gly Leu Ala Trp Gly Pro
1 5 10 15

Leu Val Leu Gly Leu Phe Gly Leu Leu Ala Ala Ser Gln Pro Gln Ala
20 25 30

Val Pro Pro Tyr Ala Ser Glu Asn Gln Thr Cys Arg Asp Gln Glu Lys
35 40 45

Glu Tyr Tyr Glu Pro Gln His Arg Ile Cys Cys Ser Arg Cys Pro Pro
50 55 60

Gly Thr Tyr Val Ser Ala Lys Cys Ser Arg Ile Arg Asp Thr Val Cys
65 70 75 80

Ala Thr Cys Ala Glu Asn Ser Tyr Asn Glu His Trp Asn Tyr Leu Thr
85 90 95

Ile Cys Gln Leu Cys Arg Pro Cys Asp Pro Val Met Gly Leu Glu Glu
100 105 110

Ile Ala Pro Cys Thr Ser Lys Arg Lys Thr Gln Cys Arg Cys Gln Pro
115 120 125

Gly Met Phe Cys Ala Ala Trp Ala Leu Glu Cys Thr His Cys Glu Leu
130 135 140

Leu Ser Asp Cys Pro Pro Gly Thr Glu Ala Glu Leu Lys Asp Glu Val
145 150 155 160

Gly Lys Gly Asn Asn His Cys Val Pro Cys Lys Ala Gly His Phe Gln
165 170 175

Asn Thr Ser Ser Pro Ser Ala Arg Cys Gln Pro His Thr Arg Cys Glu
180 185 190

Asn Gln Gly Leu Val Glu Ala Ala Pro Gly Thr Ala Gln Ser Asp Thr
195 200 205

Thr Cys Lys Asn Pro Leu Glu Pro Leu Pro Pro Glu Met Ser Glu Pro
210 215 220

Ala Leu Ser Lys Gly Val Glu Asn Leu Gln Ala Leu Leu Tyr Gln Ala
225 230 235 240

Ala Thr Gly Ser Ser Glu Ala Ser Phe Pro Thr Leu Ser Pro Leu Tyr
245 250 255

Thr Pro Pro Gln Val Gln Val Gln Gln Gly Asn Pro Glu Leu Leu Tyr
260 265 270

Ser Ser Pro Ser Val Gln Trp Leu Arg Pro Gln Lys Cys Gly Ser Ser
275 280 285

Leu Cys Leu Phe Thr Thr Pro Ser Pro Thr Leu Pro Tyr Cys Leu Pro
290 295 300

Ile Pro Leu Pro Asp Leu Glu Asn Gln Leu Pro Lys Leu Pro Ser Cys
305 310 315 320

Thr His Lys Pro Ala Gln Ser Trp Ser Leu Ser Arg Arg Ala Pro Thr
325 330 335

Pro Pro Pro Asn Met Pro Ile His Asp Thr Val Ser Pro Gly Cys Gln
340 345 350

Glu Val Leu Lys Ser Asn Leu Val Pro Leu Leu Tyr Asn Pro Arg Glu
355 360 365

Val Ser Leu Ile Leu Pro Leu Gly Ala Ala Leu Cys Leu Glu Gly Lys
370 375 380

Lys Leu Leu Pro Phe Leu Cys Leu Gly Cys Pro Gly Ile Trp Lys Ala

385 390 395 400

Leu Pro Ser Pro Pro Pro Ser Ala Leu Leu Gly Ala Val Ile Thr Leu
405 410 415

Leu Ser Ala Val Leu Ala Gly Thr Met Leu Met Leu Ala Val Leu Leu
420 425 430

Pro Leu Ala Phe Phe Leu Leu Leu Ala Thr Val Phe Ser Cys Ile Trp
435 440 445

Lys Ser His Pro Ser Leu Cys Arg Lys Leu Gly Ser Leu Leu Lys Arg
450 455 460

Arg Pro Gln Gly Glu Gly Pro Asn Pro Val Ala Gly Ser Trp Glu Pro
465 470 475 480

Pro Lys Ala His Pro Tyr Phe Pro Asp Leu Val Gln Pro Leu Leu Pro
485 490 495

Ile Ser Gly Asp Val Ser Pro Val Ser Thr Gly Leu Pro Ala Ala Pro
500 505 510

Val Leu Glu Ala Gly Val Pro Gln Gln Gln Ser Pro Leu Asp Leu Thr
515 520 525

Arg Glu Pro Gln Leu Glu Pro Gly Glu Gln Ser Gln Val Ala His Gly
530 535 540

Thr Asn Gly Ile His Val Thr Gly Gly Ser Met Thr Ile Thr Gly Asn
545 550 555 560

Ile Tyr Ile Tyr Asn Gly Pro Val Leu Gly Gly Pro Pro Gly Pro Gly
565 570 575

Asp Leu Pro Ala Thr Pro Glu Pro Pro Tyr Pro Ile Pro Glu Glu Gly
580 585 590

Asp Pro Gly Pro Pro Gly Leu Ser Thr Pro His Gln Glu Asp Gly Lys
595 600 605

Ala Trp His Leu Ala Glu Thr Glu His Cys Gly Ala Thr Pro Ser Asn
610 615 620

Arg Gly Pro Arg Asn Gln Phe Ile Thr His Asp
625 630 635

<210> 193
<211> 166
<212> PRT
<213> Homo sapien

<400> 193

Met Leu Leu Pro Trp Ala Thr Ser Ala Pro Gly Leu Ala Trp Gly Pro
1 5 10 15

Leu Val Leu Gly Leu Phe Gly Leu Leu Ala Ala Ser Gln Pro Gln Ala
20 25 30

Val Pro Pro Tyr Ala Ser Glu Asn Gln Thr Cys Arg Asp Gln Glu Lys
35 40 45

Glu Tyr Tyr Glu Pro Gln His Arg Ile Cys Cys Ser Arg Cys Pro Pro
50 55 60

Gly Thr Tyr Val Ser Ala Lys Cys Ser Arg Ile Arg Asp Thr Val Cys
65 70 75 80

Ala Thr Cys Ala Glu Asn Ser Tyr Asn Glu His Trp Asn Tyr Leu Thr
85 90 95

Ile Cys Gln Leu Cys Arg Pro Cys Asp Pro Val Met Gly Leu Glu Glu
100 105 110

Ile Ala Pro Cys Thr Ser Lys Arg Lys Thr Gln Cys Arg Cys Gln Pro
115 120 125

Gly Met Phe Cys Ala Ala Trp Ala Leu Glu Cys Thr His Cys Glu Leu
130 135 140

Leu Ser Asp Cys Pro Pro Gly Thr Glu Ala Glu Leu Lys Gly Gln Arg
145 150 155 160

Ser Leu Arg Gly Trp Met
165

<210> 194
<211> 305
<212> PRT
<213> Homo sapien

<400> 194

Gly Leu Lys Glu Thr His Arg Pro Ala Lys Gly Pro Ser Leu Leu Pro

1 5 10 15

Ile His Pro Gly Trp Pro Ala Phe Leu Leu Pro Asp Glu Val Gly Lys
20 25 30

Gly Asn Asn His Cys Val Pro Cys Lys Ala Gly His Phe Gln Asn Thr
35 40 45

Ser Ser Pro Ser Ala Arg Cys Gln Pro His Thr Arg Cys Glu Asn Gln
50 55 60

Gly Leu Val Glu Ala Ala Pro Gly Thr Ala Gln Ser Asp Thr Thr Cys
65 70 75 80

Lys Asn Pro Leu Glu Pro Leu Pro Pro Glu Met Ser Gly Thr Met Leu
85 90 95

Met Leu Ala Val Leu Leu Pro Leu Ala Phe Phe Leu Leu Leu Ala Thr
100 105 110

Val Phe Ser Cys Ile Trp Lys Ser His Pro Ser Leu Cys Arg Lys Leu
115 120 125

Gly Ser Leu Leu Lys Arg Arg Pro Gln Gly Glu Gly Pro Asn Pro Val
130 135 140

Ala Gly Ser Trp Glu Pro Pro Lys Ala His Pro Tyr Phe Pro Asp Leu
145 150 155 160

Val Gln Pro Leu Leu Pro Ile Ser Gly Asp Val Ser Pro Val Ser Thr
165 170 175

Gly Leu Pro Ala Ala Pro Val Leu Glu Ala Gly Val Pro Gln Gln Gln
180 185 190

Ser Pro Leu Asp Leu Thr Arg Glu Pro Gln Leu Glu Pro Gly Glu Gln
195 200 205

Ser Gln Val Ala His Gly Thr Asn Gly Ile His Val Thr Gly Gly Ser
210 215 220

Met Thr Ile Thr Gly Asn Ile Tyr Ile Tyr Asn Gly Pro Val Leu Gly
225 230 235 240

Gly Pro Pro Gly Pro Gly Asp Leu Pro Ala Thr Pro Glu Pro Pro Tyr
245 250 255

Pro Ile Pro Glu Glu Gly Asp Pro Gly Pro Pro Gly Leu Ser Thr Pro
260 265 270

His Gln Glu Asp Gly Lys Ala Trp His Leu Ala Glu Thr Glu His Cys
275 280 285

Gly Ala Thr Pro Ser Asn Arg Gly Pro Arg Asn Gln Phe Ile Thr His
290 295 300

Asp
305

<210> 195
<211> 194
<212> PRT
<213> Homo sapien

<400> 195

Lys Lys Arg Glu Gly Gly Arg Glu Lys Lys Gly Ser Gly Ala Leu Ile
1 5 10 15

Ile Val Trp Val Ser Ile Ser Phe Leu Gln Gly Glu Gly Pro Asn Pro
20 25 30

Val Ala Gly Ser Trp Glu Pro Pro Lys Ala His Pro Tyr Phe Pro Asp
35 40 45

Leu Val Gln Pro Leu Leu Pro Ile Ser Gly Asp Val Ser Pro Val Ser
50 55 60

Thr Gly Leu Pro Ala Ala Pro Val Leu Glu Ala Gly Val Pro Gln Gln
65 70 75 80

Gln Ser Pro Leu Asp Leu Thr Arg Glu Pro Gln Leu Glu Pro Gly Glu
85 90 95

Gln Ser Gln Val Ala His Gly Thr Asn Gly Ile His Val Thr Gly Gly
100 105 110

Ser Met Thr Ile Thr Gly Asn Ile Tyr Ile Tyr Asn Gly Pro Val Leu
115 120 125

Gly Gly Pro Pro Gly Pro Gly Asp Leu Pro Ala Thr Pro Glu Pro Pro
130 135 140

Tyr Pro Ile Pro Glu Glu Gly Asp Pro Gly Pro Pro Gly Leu Ser Thr
145 150 155 160

Pro His Gln Glu Asp Gly Lys Ala Trp His Leu Ala Glu Thr Glu His
165 170 175

Cys Gly Ala Thr Pro Ser Asn Arg Gly Pro Arg Asn Gln Phe Ile Thr
180 185 190

His Asp

<210> 196
<211> 241
<212> PRT
<213> Homo sapien

<400> 196

Met Ala Thr Gly Leu Ser Glu His His Asn Met Val Trp Glu Val Lys
1 5 10 15

Thr Asn Gln Met Pro Asn Ala Val Gln Lys Leu Leu Leu Val Met Asp
20 25 30

Lys Arg Ala Ser Gly Met Asn Asp Ser Leu Glu Leu Leu Gln Cys Asn
35 40 45

Glu Asn Leu Pro Ser Ser Pro Gly Tyr Asn Ser Cys Asp Glu His Met
50 55 60

Glu Leu Asp Asp Leu Pro Glu Leu Gln Ala Val Gln Ser Asp Pro Thr
65 70 75 80

Gln Ser Gly Met Tyr Gln Leu Ser Ser Asp Val Ser His Gln Glu Tyr
85 90 95

Pro Arg Ser Ser Trp Asn Gln Asn Thr Ser Asp Ile Pro Glu Thr Thr
100 105 110

Tyr Arg Glu Asn Glu Val Asp Trp Leu Thr Glu Leu Ala Asn Ile Ala
115 120 125

Thr Ser Pro Gln Ser Pro Leu Met Gln Cys Ser Phe Tyr Asn Arg Ser
130 135 140

Ser Pro Val His Ile Ile Ala Thr Ser Lys Ser Leu His Ser Tyr Ala
145 150 155 160

Arg Pro Pro Pro Val Ser Ser Ser Ser Lys Ser Glu Pro Ala Phe Pro
165 170 175

His His His Trp Lys Glu Glu Thr Pro Val Arg His Glu Arg Ala Asn
180 185 190

Ser Glu Ser Glu Ser Gly Ile Phe Cys Met Ser Ser Leu Ser Asp Asp
195 200 205

Asp Asp Leu Gly Trp Cys Asn Ser Trp Pro Ser Thr Val Trp His Cys
210 215 220

Phe Leu Lys Ala Met Thr Ser His Leu Trp Ile Leu Leu Gln Phe Met
225 230 235 240

Cys

<210> 197
<211> 261
<212> PRT
<213> Homo sapien

<400> 197

Met Thr Gly Leu Ala Leu Leu Tyr Ser Gly Val Phe Val Ala Phe Trp
1 5 10 15

Ala Cys Ala Leu Ala Val Gly Val Cys Tyr Thr Ile Phe Asp Leu Gly
20 25 30

Phe Arg Phe Asp Val Ala Trp Phe Leu Thr Glu Thr Ser Pro Phe Met
35 40 45

Trp Ser Asn Leu Gly Ile Gly Leu Ala Ile Ser Leu Ser Val Val Gly
50 55 60

Ala Ala Trp Gly Ile Tyr Ile Thr Gly Ser Ser Ile Ile Gly Gly Gly
65 70 75 80

Val Lys Ala Pro Arg Ile Lys Thr Lys Asn Leu Val Ser Ile Ile Phe
85 90 95

Cys Glu Ala Val Ala Ile Tyr Gly Ile Ile Met Ala Ile Val Ile Ser
100 105 110

Asn Met Ala Glu Pro Phe Ser Ala Thr Asp Pro Lys Ala Ile Gly His
115 120 125

Arg Asn Tyr His Ala Gly Tyr Ser Met Phe Gly Ala Gly Leu Thr Val
130 135 140

Gly Leu Ser Asn Leu Phe Cys Gly Val Cys Val Gly Ile Val Gly Ser
145 150 155 160

Gly Ala Ala Leu Ala Asp Ala Gln Asn Pro Ser Leu Phe Val Lys Ile
165 170 175

Leu Ile Val Glu Ile Phe Gly Ser Ala Ile Gly Leu Phe Gly Val Ile
180 185 190

Val Ala Ile Leu Gln Val Met Asn Pro Leu Gly Lys Pro Leu Cys Pro
195 200 205

Cys Pro Gln Pro Ser Leu Thr Leu Leu Leu Glu Lys Leu Lys Cys Ser
210 215 220

Pro Ser Leu Pro Ile Thr Ile Asp Ser Pro Lys Gln Leu Pro Pro Pro
225 230 235 240

His Phe His Leu Leu Val Phe Ser Tyr Arg Gly Ser Leu Phe Leu Ser
245 250 255

Leu Ile Trp Cys His
260

<210> 198
<211> 499
<212> PRT
<213> Homo sapien

<400> 198

Met Ala Pro Ala Arg Thr Met Ala Arg Ala Arg Leu Ala Pro Ala Gly
1 5 10 15

Ile Pro Ala Val Ala Leu Trp Leu Leu Cys Thr Leu Gly Leu Gln Gly
20 25 30

Thr Gln Ala Gly Pro Pro Pro Ala Pro Pro Gly Leu Pro Ala Gly Ala
35 40 45

Asp Cys Leu Asn Ser Phe Thr Ala Gly Val Pro Gly Phe Val Leu Asp
50 55 60

Thr Asn Ala Ser Val Ser Asn Gly Ala Thr Phe Leu Glu Ser Pro Thr
65 70 75 80

Val Arg Arg Gly Trp Asp Cys Val Arg Ala Cys Cys Thr Thr Gln Asn
85 90 95

Cys Asn Leu Ala Leu Val Glu Leu Gln Pro Asp Arg Gly Glu Asp Ala
100 105 110

Ile Ala Ala Cys Phe Leu Ile Asn Cys Leu Tyr Glu Gln Asn Phe Val
115 120 125

Cys Lys Phe Ala Pro Arg Glu Gly Phe Ile Asn Tyr Leu Thr Arg Glu
130 135 140

Val Tyr Arg Ser Tyr Arg Gln Leu Arg Thr Gln Gly Phe Gly Gly Ser
145 150 155 160

Gly Ile Pro Lys Ala Trp Ala Gly Ile Asp Leu Lys Val Gln Pro Gln
165 170 175

Glu Pro Leu Val Leu Lys Asp Val Glu Asn Thr Asp Trp Arg Leu Leu
180 185 190

Arg Gly Asp Thr Asp Val Arg Val Glu Arg Lys Asp Pro Asn Gln Val
195 200 205

Glu Leu Trp Gly Leu Lys Glu Gly Thr Tyr Leu Phe Gln Leu Thr Val
210 215 220

Thr Ser Ser Asp His Pro Glu Asp Thr Ala Asn Val Thr Val Thr Val
225 230 235 240

Leu Ser Thr Lys Gln Thr Glu Asp Tyr Cys Leu Ala Ser Asn Lys Val
245 250 255

Gly Arg Cys Arg Gly Ser Phe Pro Arg Trp Tyr Tyr Asp Pro Thr Glu
260 265 270

Gln Ile Cys Lys Ser Phe Val Tyr Gly Gly Cys Leu Gly Asn Lys Asn
275 280 285

Asn Tyr Leu Arg Glu Glu Glu Cys Ile Leu Ala Cys Arg Gly Val Gln
290 295 300

Gly Gly Pro Leu Arg Gly Ser Ser Gly Ala Gln Ala Thr Phe Pro Gln
305 310 315 320

Gly Pro Ser Met Glu Arg Arg His Pro Val Cys Ser Gly Thr Cys Gln
325 330 335

Pro Thr Gln Phe Arg Cys Ser Asn Gly Cys Cys Ile Asp Ser Phe Leu
340 345 350

Glu Cys Asp Asp Thr Pro Asn Cys Pro Asp Ala Ser Asp Glu Ala Ala
355 360 365

Cys Glu Lys Tyr Thr Ser Gly Phe Asp Glu Leu Gln Arg Ile His Phe
370 375 380

Pro Ser Asp Lys Gly His Cys Val Asp Leu Pro Asp Thr Gly Leu Cys
385 390 395 400

Lys Glu Ser Ile Pro Arg Trp Tyr Tyr Asn Pro Phe Ser Glu His Cys
405 410 415

Ala Arg Phe Thr Tyr Gly Gly Cys Tyr Gly Asn Lys Asn Asn Phe Glu
420 425 430

Glu Glu Gln Gln Cys Leu Glu Ser Cys Arg Gly Ile Ser Ser Glu Trp
435 440 445

Ala Ser Glu Arg Val Gly Met Tyr Gly Gly Arg Leu Ser Gln Trp Pro
450 455 460

Pro Leu Cys Pro Gln Ala Phe Gly Ser His Pro Ser Ile Leu Arg Ala
465 470 475 480

Pro Gly Val Gly Val Gly Glu Asp Ala Ser Val Arg Ser Gly Ala Leu
485 490 495

Gly Ser Ser

<210> 199
<211> 344
<212> PRT
<213> Homo sapien

<400> 199

Met Ala Pro Ala Arg Thr Met Ala Arg Ala Arg Leu Ala Pro Ala Gly

251

1 5 10 15

Ile Pro Ala Val Ala Leu Trp Leu Leu Cys Thr Leu Gly Leu Gln Gly
20 25 30

Thr Gln Ala Gly Pro Pro Pro Ala Pro Pro Gly Leu Pro Ala Gly Ala
35 40 45

Asp Cys Leu Asn Ser Phe Thr Ala Gly Val Pro Gly Phe Val Leu Asp
50 55 60

Thr Asn Ala Ser Val Ser Asn Gly Ala Thr Phe Leu Glu Ser Pro Thr
65 70 75 80

Val Arg Arg Gly Trp Asp Cys Val Arg Ala Cys Cys Thr Thr Gln Asn
85 90 95

Cys Asn Leu Ala Leu Val Glu Leu Gln Pro Asp Arg Gly Glu Asp Ala
100 105 110

Ile Ala Ala Cys Phe Leu Ile Asn Cys Leu Tyr Glu Gln Asn Phe Val
115 120 125

Cys Lys Phe Ala Pro Arg Glu Gly Phe Ile Asn Tyr Leu Thr Arg Glu
130 135 140

Val Tyr Arg Ser Tyr Arg Gln Leu Arg Thr Gln Gly Phe Gly Gly Ser
145 150 155 160

Gly Ile Pro Lys Ala Trp Ala Gly Ile Asp Leu Lys Val Gln Pro Gln
165 170 175

Glu Pro Leu Val Leu Lys Asp Val Glu Asn Thr Asp Trp Arg Leu Leu
180 185 190

Arg Gly Asp Thr Asp Val Arg Val Glu Arg Lys Asp Pro Asn Gln Val
195 200 205

Glu Leu Trp Gly Leu Lys Glu Gly Thr Tyr Leu Phe Gln Leu Thr Val
210 215 220

Thr Ser Ser Asp His Pro Glu Asp Thr Ala Asn Val Thr Val Thr Val
225 230 235 240

Leu Ser Thr Lys Gln Thr Glu Asp Tyr Cys Leu Ala Ser Asn Lys Val
245 250 255

Gly Arg Cys Arg Gly Ser Phe Pro Arg Trp Tyr Tyr Asp Pro Thr Glu
260 265 270

Gln Ile Cys Lys Ser Phe Val Tyr Gly Gly Cys Leu Gly Asn Lys Asn
275 280 285

Asn Tyr Leu Arg Glu Glu Glu Cys Ile Leu Ala Cys Arg Gly Val Gln
290 295 300

Gly Gly Pro Leu Arg Gly Ser Ser Gly Ala Gln Ala Thr Phe Pro Gln
305 310 315 320

Gly Pro Ser Met Glu Arg Arg His Pro Gly Gly Leu Tyr Ser Pro Pro
325 330 335

His Pro Pro Ser Pro Pro His Leu
340

<210> 200
<211> 479
<212> PRT
<213> Homo sapien

<400> 200

Arg Asn Gln Gly Glu Lys Ala Ala Glu Pro Gln Leu Ser Glu His Arg
1 5 10 15

Val Gly Ser Arg Asp Pro Ser Arg Ala Gly Ser Trp Asp Arg Asn Leu
20 25 30

Gly Gly Pro Gly Pro Thr Gln Leu Thr Cys Ala Gly His Gln His Pro
35 40 45

Arg Asn Pro Glu Ala Arg Ala Leu Lys Val Thr Pro Leu Gly Arg Lys
50 55 60

Ala Met Ala Pro Ala Arg Thr Met Ala Arg Ala Arg Leu Ala Pro Ala
65 70 75 80

Gly Ile Pro Ala Val Ala Leu Trp Leu Leu Cys Thr Leu Gly Leu Gln
85 90 95

Gly Thr Gln Ala Gly Pro Pro Pro Ala Pro Pro Gly Leu Pro Ala Gly
100 105 110

Ala Asp Cys Leu Asn Ser Phe Thr Ala Gly Val Pro Gly Phe Val Leu
115 120 125

Asp Thr Asn Ala Ser Val Ser Asn Gly Ala Thr Phe Leu Glu Ser Pro
130 135 140

Thr Val Arg Arg Gly Trp Asp Cys Val Arg Ala Cys Cys Thr Thr Gln
145 150 155 160

Asn Cys Asn Leu Ala Leu Val Glu Leu Gln Pro Asp Arg Gly Glu Asp
165 170 175

Ala Ile Ala Ala Cys Phe Leu Ile Asn Cys Leu Tyr Glu Gln Asn Phe
180 185 190

Val Cys Lys Phe Ala Pro Arg Glu Gly Phe Ile Asn Tyr Leu Thr Arg
195 200 205

Glu Val Tyr Arg Ser Tyr Arg Gln Leu Arg Thr Gln Gly Phe Gly Gly
210 215 220

Ser Gly Ile Pro Lys Ala Trp Ala Gly Ile Asp Leu Lys Val Gln Pro
225 230 235 240

Gln Glu Pro Leu Val Leu Lys Asp Val Glu Asn Thr Asp Trp Arg Leu
245 250 255

Leu Arg Gly Asp Thr Asp Val Arg Val Glu Arg Lys Asp Pro Asn Gln
260 265 270

Val Glu Leu Trp Gly Leu Lys Glu Gly Thr Tyr Leu Phe Gln Leu Thr
275 280 285

Val Thr Ser Ser Asp His Pro Glu Asp Thr Ala Asn Val Thr Val Thr
290 295 300

Val Leu Ser Thr Lys Gln Thr Glu Asp Tyr Cys Leu Ala Ser Asn Lys
305 310 315 320

Val Gly Arg Cys Arg Gly Ser Phe Pro Arg Trp Tyr Tyr Asp Pro Thr
325 330 335

Glu Gln Ile Cys Lys Ser Phe Val Tyr Gly Gly Cys Leu Gly Asn Lys
340 345 350

Asn Asn Tyr Leu Arg Glu Glu Glu Cys Ile Leu Ala Cys Arg Gly Val

355 360 365

Gln Gly Gly Pro Leu Arg Gly Ser Ser Gly Ala Gln Ala Thr Phe Pro
370 375 380

Gln Gly Pro Ser Met Glu Arg Arg His Pro Val Cys Ser Gly Thr Cys
385 390 395 400

Gln Pro Thr Gln Phe Arg Cys Ser Asn Gly Cys Cys Ile Asp Ser Phe
405 410 415

Leu Glu Cys Asp Asp Thr Pro Asn Cys Pro Asp Ala Ser Asp Glu Ala
420 425 430

Ala Cys Glu Lys Tyr Thr Ser Gly Phe Asp Glu Leu Gln Arg Ile His
435 440 445

Phe Pro Ser Asp Lys Gly Glu Ile Leu Pro Arg Cys Pro Gly Ser Gly
450 455 460

Gln Thr Leu Thr Leu Pro Ser Ser Leu Phe Pro Ser Ser Ser Ala
465 470 475

<210> 201
<211> 121
<212> PRT
<213> Homo sapien

<400> 201

Met Val Arg Ile Leu Ala Asn Gly Glu Ile Val Gln Asp Asp Asp Pro
1 5 10 15

Arg Val Arg Thr Thr Thr Gln Pro Pro Arg Gly Ser Ile Pro Arg Gln
20 25 30

Ser Phe Phe Asn Arg Gly His Gly Ala Pro Pro Gly Gly Pro Gly Pro
35 40 45

Arg Gln Gln Gln Ala Gly Ala Arg Leu Gly Ala Ala Gln Ser Pro Phe
50 55 60

Asn Asp Leu Asn Arg Gln Leu Val Asn Met Gly Phe Pro Gln Trp His
65 70 75 80

Leu Gly Asn His Ala Val Glu Pro Val Thr Ser Ile Leu Leu Leu Phe
85 90 95

Leu Leu Met Met Leu Gly Val Arg Gly Leu Leu Leu Val Gly Leu Val
100 105 110

Tyr Leu Val Ser His Leu Ser Gln Arg
115 120

<210> 202
<211> 149
<212> PRT
<213> Homo sapien

<400> 202

Glu Gln Ala Tyr Leu Glu Gly Ile Trp Trp Cys Leu Glu Gly Met Ile
1 5 10 15

Arg Glu Gly Thr Thr Gly Val Cys Phe Pro Phe Val Leu Ser Val Arg
20 25 30

Gln Arg Glu Thr Leu Val Gln His Phe Gln Ser Val Gly Gly Ser Val
35 40 45

Gly Ser Arg Asp Thr Phe Arg Trp Tyr Gly Ala Cys Ile Lys Trp His
50 55 60

Lys Ile Arg Ala Arg Lys Arg Cys Pro Ser Gln Phe Ser Gln Ser Phe
65 70 75 80

Tyr Ala Glu Lys Ile Ser Ala Gly Cys Gln His Val Pro Met Pro Val
85 90 95

Glu Asp Met Pro Thr Ser Pro Leu Pro Arg Glu Gln Asp Leu Gly Leu
100 105 110

Gly Gln Val Glu Lys Ile Pro Asp Phe Phe Ser Thr Val Phe Val Leu
115 120 125

Met Val Tyr Phe Tyr Trp Leu Leu Tyr Cys Leu Gly Gln Val Val Val
130 135 140

Ala Phe Tyr Leu Leu
145

<210> 203
<211> 121
<212> PRT
<213> Homo sapien

<400> 203

Met Val Arg Ile Leu Ala Asn Gly Glu Ile Val Gln Asp Asp Asp Pro
1 5 10 15

Arg Val Arg Thr Thr Thr Gln Pro Pro Arg Gly Ser Ile Pro Arg Gln
20 25 30

Ser Phe Phe Asn Arg Gly His Gly Ala Pro Pro Gly Gly Pro Gly Pro
35 40 45

Arg Gln Gln Gln Ala Gly Ala Arg Leu Gly Ala Ala Gln Ser Pro Phe
50 55 60

Asn Asp Leu Asn Arg Gln Leu Val Asn Met Gly Phe Pro Gln Trp His
65 70 75 80

Leu Gly Asn His Ala Val Glu Pro Val Thr Ser Ile Leu Leu Leu Phe
85 90 95

Leu Leu Met Met Leu Gly Val Arg Gly Leu Leu Leu Val Gly Leu Val
100 105 110

Tyr Leu Val Ser His Leu Ser Gln Arg
115 120

<210> 204
<211> 149
<212> PRT
<213> Homo sapien

<400> 204

Glu Gln Ala Tyr Leu Glu Gly Ile Trp Trp Cys Leu Glu Gly Met Ile
1 5 10 15

Arg Glu Gly Thr Thr Gly Val Cys Phe Pro Phe Val Leu Ser Val Arg
20 25 30

Gln Arg Glu Thr Leu Val Gln His Phe Gln Ser Val Gly Gly Ser Val
35 40 45

Gly Ser Arg Asp Thr Phe Arg Trp Tyr Gly Ala Cys Ile Lys Trp His
50 55 60

Lys Ile Arg Ala Arg Lys Arg Cys Pro Ser Gln Phe Ser Gln Ser Phe
65 70 75 80

Tyr Ala Glu Lys Ile Ser Ala Gly Cys Gln His Val Pro Met Pro Val
85 90 95

Glu Asp Met Pro Thr Ser Pro Leu Pro Arg Glu Gln Asp Leu Gly Leu
100 105 110

Gly Gln Val Glu Lys Ile Pro Asp Phe Phe Ser Thr Val Phe Val Leu
115 120 125

Met Val Tyr Phe Tyr Trp Leu Leu Tyr Cys Leu Gly Gln Val Val Val
130 135 140

Ala Phe Tyr Leu Leu
145

<210> 205
<211> 101
<212> PRT
<213> Homo sapien

<400> 205

Met Ile His Ser Ser Leu Ser Val Phe Thr Phe Gln Ser Phe Phe Asn
1 5 10 15

Arg Gly His Gly Ala Pro Pro Gly Gly Pro Gly Pro Arg Gln Gln Gln
20 25 30

Ala Gly Ala Arg Leu Gly Ala Ala Gln Ser Pro Phe Asn Asp Leu Asn
35 40 45

Arg Gln Leu Val Asn Met Gly Phe Pro Gln Trp His Leu Gly Asn His
50 55 60

Ala Val Glu Pro Val Thr Ser Ile Leu Leu Leu Phe Leu Leu Met Met
65 70 75 80

Leu Gly Val Arg Gly Leu Leu Leu Val Gly Leu Val Tyr Leu Val Ser
85 90 95

His Leu Ser Gln Arg
100

<210> 206
<211> 95
<212> PRT
<213> Homo sapien

<400> 206

Trp Ile Ala Arg Ala Gly Thr Gln Leu Gln Asn Phe Thr Leu Asp Arg
1 5 10 15

Ser Ser Val Leu Val Asp Gly Tyr Ser Pro Asn Arg Asn Glu Pro Leu
20 25 30

Thr Gly Asn Ser Asp Leu Pro Phe Trp Ala Val Ile Leu Ile Gly Leu
35 40 45

Ala Gly Leu Leu Gly Leu Ile Thr Cys Leu Ile Cys Gly Val Leu Val
50 55 60

Thr Thr Arg Arg Arg Lys Lys Glu Gly Glu Tyr Asn Val Gln Gln Gln
65 70 75 80

Cys Pro Gly Tyr Tyr Gln Ser His Leu Asp Leu Glu Asp Leu Gln
85 90 95

<210> 207
<211> 109
<212> PRT
<213> Homo sapien

<400> 207

Met His Ala Arg Ala Ala Gln Cys Asp Gly Ser Val Val Ala Ala Asp
1 5 10 15

Pro Gly Asp Gly Thr Gln Leu Gln Asn Phe Thr Leu Asp Arg Ser Ser
20 25 30

Val Leu Val Asp Gly Tyr Ser Pro Asn Arg Asn Glu Pro Leu Thr Gly
35 40 45

Asn Ser Asp Leu Pro Phe Trp Ala Val Ile Leu Ile Gly Leu Ala Gly
50 55 60

Leu Leu Gly Leu Ile Thr Cys Leu Ile Cys Gly Val Leu Val Thr Thr
65 70 75 80

Arg Arg Arg Lys Lys Glu Gly Glu Tyr Asn Val Gln Gln Gln Cys Pro
85 90 95

Gly Tyr Tyr Gln Ser His Leu Asp Leu Glu Asp Leu Gln
100 105

<210> 208

<211> 1485
<212> PRT
<213> Homo sapien

<400> 208

Met Gln His Pro Gly Ser Arg Lys Phe Asn Thr Thr Glu Arg Val Leu
1 5 10 15

Gln Gly Leu Leu Lys Pro Leu Phe Lys Ser Thr Ser Val Gly Pro Leu
20 25 30

Tyr Ser Gly Cys Arg Leu Thr Leu Leu Arg Pro Glu Lys His Gly Ala
35 40 45

Ala Thr Gly Val Asp Ala Ile Cys Thr Leu Arg Leu Asp Pro Thr Gly
50 55 60

Pro Gly Leu Asp Arg Glu Arg Leu Tyr Trp Glu Leu Ser Gln Leu Thr
65 70 75 80

Asn Ser Val Thr Glu Leu Gly Pro Tyr Thr Leu Asp Arg Asp Ser Leu
85 90 95

Tyr Val Asn Gly Phe Thr His Arg Ser Ser Val Pro Thr Thr Ser Ile
100 105 110

Pro Gly Thr Ser Ala Val His Leu Glu Thr Ser Gly Thr Pro Ala Ser
115 120 125

Leu Pro Gly His Thr Ala Pro Gly Pro Leu Leu Val Pro Phe Thr Leu
130 135 140

Asn Phe Thr Ile Thr Asn Leu Gln Tyr Glu Glu Asp Met Arg His Pro
145 150 155 160

Gly Ser Arg Lys Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu
165 170 175

Lys Pro Leu Phe Lys Ser Thr Ser Val Gly Pro Leu Tyr Ser Gly Cys
180 185 190

Arg Leu Thr Leu Leu Arg Pro Glu Lys Arg Gly Ala Ala Thr Gly Val
195 200 205

Asp Thr Ile Cys Thr His Arg Leu Asp Pro Leu Asn Pro Gly Leu Asp
210 215 220

Arg Glu Gln Leu Tyr Trp Glu Leu Ser Lys Leu Thr Arg Gly Ile Ile
225 230 235 240

Glu Leu Gly Pro Tyr Leu Leu Asp Arg Gly Ser Leu Tyr Val Asn Gly
245 250 255

Phe Thr His Arg Asn Phe Val Pro Ile Thr Ser Thr Pro Gly Thr Ser
260 265 270

Thr Val His Leu Gly Thr Ser Glu Thr Pro Ser Ser Leu Pro Arg Pro
275 280 285

Ile Val Pro Gly Pro Leu Leu Val Pro Phe Thr Leu Asn Phe Thr Ile
290 295 300

Thr Asn Leu Gln Tyr Glu Glu Ala Met Arg His Pro Gly Ser Arg Lys
305 310 315 320

Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu Arg Pro Leu Phe
325 330 335

Lys Asn Thr Ser Ile Gly Pro Leu Tyr Ser Ser Cys Arg Leu Thr Leu
340 345 350

Leu Arg Pro Glu Lys Asp Lys Ala Ala Thr Arg Val Asp Ala Ile Cys
355 360 365

Thr His His Pro Asp Pro Gln Ser Pro Gly Leu Asn Arg Glu Gln Leu
370 375 380

Tyr Trp Glu Leu Ser Gln Leu Thr His Gly Ile Thr Glu Leu Gly Pro
385 390 395 400

Tyr Thr Leu Asp Arg Asp Ser Leu Tyr Val Asp Gly Phe Thr His Trp
405 410 415

Ser Pro Ile Pro Thr Thr Ser Thr Pro Gly Thr Ser Ile Val Asn Leu
420 425 430

Gly Thr Ser Gly Ile Pro Pro Ser Leu Pro Glu Thr Thr Ala Thr Gly
435 440 445

Pro Leu Leu Val Pro Phe Thr Leu Asn Phe Thr Ile Thr Asn Leu Gln
450 455 460

Tyr Glu Glu Asn Met Gly His Pro Gly Ser Arg Lys Phe Asn Ile Thr
465 470 475 480

Glu Ser Val Leu Gln Gly Leu Leu Lys Pro Leu Phe Lys Ser Thr Ser
485 490 495

Val Gly Pro Leu Tyr Ser Gly Cys Arg Leu Thr Leu Leu Arg Pro Glu
500 505 510

Lys Asp Gly Val Ala Thr Arg Val Asp Ala Ile Cys Thr His Arg Pro
515 520 525

Asp Pro Lys Ile Pro Gly Leu Asp Arg Gln Gln Leu Tyr Trp Glu Leu
530 535 540

Ser Gln Leu Thr His Ser Ile Thr Glu Leu Gly Pro Tyr Thr Leu Asp
545 550 555 560

Arg Asp Ser Leu Tyr Val Asn Gly Phe Thr Gln Arg Ser Ser Val Pro
565 570 575

Thr Thr Ser Thr Pro Gly Thr Phe Thr Val Gln Pro Glu Thr Ser Glu
580 585 590

Thr Pro Ser Ser Leu Pro Gly Pro Thr Ala Thr Gly Pro Val Leu Leu
595 600 605

Pro Phe Thr Leu Asn Phe Thr Ile Ile Asn Leu Gln Tyr Glu Glu Asp
610 615 620

Met His Arg Pro Gly Ser Arg Lys Phe Asn Thr Thr Glu Arg Val Leu
625 630 635 640

Gln Gly Leu Leu Met Pro Leu Phe Lys Asn Thr Ser Val Ser Ser Leu
645 650 655

Tyr Ser Gly Cys Arg Leu Thr Leu Leu Arg Pro Glu Lys Asp Gly Ala
660 665 670

Ala Thr Arg Val Asp Ala Val Cys Thr His Arg Pro Asp Pro Lys Ser
675 680 685

Pro Gly Leu Asp Arg Glu Arg Leu Tyr Trp Lys Leu Ser Gln Leu Thr
690 695 700

His Gly Ile Thr Glu Leu Gly Pro Tyr Thr Leu Asp Arg His Ser Leu

705 710 715 720

Tyr Val Asn Gly Phe Thr His Gln Ser Ser Met Thr Thr Thr Arg Thr
725 730 735

Pro Asp Thr Ser Thr Met His Leu Ala Thr Ser Arg Thr Pro Ala Ser
740 745 750

Leu Ser Gly Pro Thr Thr Ala Ser Pro Leu Leu Val Leu Phe Thr Ile
755 760 765

Asn Phe Thr Ile Thr Asn Leu Arg Tyr Glu Glu Asn Met His His Pro
770 775 780

Gly Ser Arg Lys Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu
785 790 795 800

Arg Pro Val Phe Lys Asn Thr Ser Val Gly Pro Leu Tyr Ser Gly Cys
805 810 815

Arg Leu Thr Leu Leu Arg Pro Lys Lys Asp Gly Ala Ala Thr Lys Val
820 825 830

Asp Ala Ile Cys Thr Tyr Arg Pro Asp Pro Lys Ser Pro Gly Leu Asp
835 840 845

Arg Glu Gln Leu Tyr Trp Glu Leu Ser Gln Leu Thr His Ser Ile Thr
850 855 860

Glu Leu Gly Pro Tyr Thr Leu Asp Arg Asp Ser Leu Tyr Val Asn Gly
865 870 875 880

Phe Thr Gln Arg Ser Ser Val Pro Thr Thr Ser Ile Pro Gly Thr Pro
885 890 895

Thr Val Asp Leu Gly Thr Ser Gly Thr Pro Val Ser Lys Pro Gly Pro
900 905 910

Ser Ala Ala Ser Pro Leu Leu Val Leu Phe Thr Leu Asn Phe Thr Ile
915 920 925

Thr Asn Leu Arg Tyr Glu Glu Asn Met Gln His Pro Gly Ser Arg Lys
930 935 940

Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu Arg Ser Leu Phe
945 950 955 960

Lys Ser Thr Ser Val Gly Pro Leu Tyr Ser Gly Cys Arg Leu Thr Leu
965 970 975

Leu Arg Pro Glu Lys Asp Gly Thr Ala Thr Gly Val Asp Ala Ile Cys
980 985 990

Thr His His Pro Asp Pro Lys Ser Pro Arg Leu Asp Arg Glu Gln Leu
995 1000 1005

Tyr Trp Glu Leu Ser Gln Leu Thr His Asn Ile Thr Glu Leu Gly
1010 1015 1020

Pro Tyr Ala Leu Asp Asn Asp Ser Leu Phe Val Asn Gly Phe Thr
1025 1030 1035

His Arg Ser Ser Val Ser Thr Thr Ser Thr Pro Gly Thr Pro Thr
1040 1045 1050

Val Tyr Leu Gly Ala Ser Lys Thr Pro Ala Ser Ile Phe Gly Pro
1055 1060 1065

Ser Ala Ala Ser His Leu Leu Ile Leu Phe Thr Leu Asn Phe Thr
1070 1075 1080

Ile Thr Asn Leu Arg Tyr Glu Glu Asn Met Trp Pro Gly Ser Arg
1085 1090 1095

Lys Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu Arg Pro
1100 1105 1110

Leu Phe Lys Asn Thr Ser Val Gly Pro Leu Tyr Ser Gly Cys Arg
1115 1120 1125

Leu Thr Leu Leu Arg Pro Glu Lys Asp Gly Glu Ala Thr Gly Val
1130 1135 1140

Asp Ala Ile Cys Thr His Arg Pro Asp Pro Thr Gly Pro Gly Leu
1145 1150 1155

Asp Arg Glu Gln Leu Tyr Leu Glu Leu Ser Gln Leu Thr His Ser
1160 1165 1170

Ile Thr Glu Leu Gly Pro Tyr Thr Leu Asp Arg Asp Ser Leu Tyr
1175 1180 1185

Val Asn Gly Phe Thr His Arg Ser Ser Val Pro Thr Thr Ser Thr
1190 1195 1200

Gly Val Val Ser Glu Glu Pro Phe Thr Leu Asn Phe Thr Ile Asn
1205 1210 1215

Asn Leu Arg Tyr Met Ala Asp Met Gly Gln Pro Gly Ser Leu Lys
1220 1225 1230

Phe Asn Ile Thr Asp Asn Val Met Lys His Leu Leu Ser Pro Leu
1235 1240 1245

Phe Gln Arg Ser Ser Leu Gly Ala Arg Tyr Thr Gly Cys Arg Val
1250 1255 1260

Ile Ala Leu Arg Ser Val Lys Asn Gly Ala Glu Thr Arg Val Asp
1265 1270 1275

Leu Leu Cys Thr Tyr Leu Gln Pro Leu Ser Gly Pro Gly Leu Pro
1280 1285 1290

Ile Lys Gln Val Phe His Glu Leu Ser Gln Gln Thr His Gly Ile
1295 1300 1305

Thr Arg Leu Gly Pro Tyr Ser Leu Asp Lys Asp Ser Leu Tyr Leu
1310 1315 1320

Asn Gly Tyr Asn Glu Pro Gly Pro Asp Glu Pro Pro Thr Thr Pro
1325 1330 1335

Lys Pro Ala Thr Thr Phe Leu Pro Pro Leu Ser Glu Ala Thr Thr
1340 1345 1350

Ala Met Gly Tyr His Leu Lys Thr Leu Thr Leu Asn Phe Thr Ile
1355 1360 1365

Ser Asn Leu Gln Tyr Ser Pro Asp Met Gly Lys Gly Ser Ala Thr
1370 1375 1380

Phe Asn Ser Thr Glu Gly Val Leu Gln His Leu Leu Arg Pro Leu
1385 1390 1395

Phe Gln Lys Ser Ser Met Gly Pro Phe Tyr Leu Gly Cys Gln Leu
1400 1405 1410

Ile Ser Leu Arg Pro Glu Lys Asp Gly Ala Ala Thr Gly Val Asp
1415 1420 1425

Thr Thr Cys Thr Tyr His Pro Asp Pro Val Gly Pro Gly Leu Asp
1430 1435 1440

Ile Gln Gln Leu Tyr Trp Glu Leu Ser Gln Leu Thr His Gly Val
1445 1450 1455

Thr Gln Leu Gly Phe Tyr Val Leu Asp Arg Asp Ser Leu Phe Ile
1460 1465 1470

Asn Gly His His Thr Leu Gln Arg Gln Ser Thr Thr
1475 1480 1485

<210> 209
<211> 111
<212> PRT
<213> Homo sapien

<220>
<221> MISC_FEATURE
<222> (11)..(12)
<223> X=any amino acid

<400> 209

Lys Lys Arg Lys Glu Arg Lys Arg Glu Asn Xaa Xaa Thr Ile Gly Thr
1 5 10 15

Gly Ser Leu Met His Ala Arg Ala Ala Gln Cys Asp Gly Ser Pro Gly
20 25 30

Arg Cys Val Leu Val Asp Gly Tyr Ser Pro Asn Arg Asn Glu Pro Leu
35 40 45

Thr Gly Asn Ser Asp Leu Pro Phe Trp Ala Val Ile Leu Ile Gly Leu
50 55 60

Ala Gly Leu Leu Gly Leu Ile Thr Cys Leu Ile Cys Gly Val Leu Val
65 70 75 80

Thr Thr Arg Arg Arg Lys Lys Glu Gly Glu Tyr Asn Val Gln Gln Gln
85 90 95

Cys Pro Gly Tyr Tyr Gln Ser His Leu Asp Leu Glu Asp Leu Gln
100 105 110

<210> 210
<211> 87
<212> PRT
<213> Homo sapien

<400> 210

Met Arg Gly Arg Gly Arg Pro Gly Arg Cys Val Leu Val Asp Gly Tyr
1 5 10 15

Ser Pro Asn Arg Asn Glu Pro Leu Thr Gly Asn Ser Asp Leu Pro Phe
20 25 30

Trp Ala Val Ile Leu Ile Gly Leu Ala Gly Leu Leu Gly Leu Ile Thr
35 40 45

Cys Leu Ile Cys Gly Val Leu Val Thr Thr Arg Arg Arg Lys Lys Glu
50 55 60

Gly Glu Tyr Asn Val Gln Gln Gln Cys Pro Gly Tyr Tyr Gln Ser His
65 70 75 80

Leu Asp Leu Glu Asp Leu Gln
85

<210> 211
<211> 92
<212> PRT
<213> Homo sapien

<400> 211

Pro Ser Leu Leu Gly Cys His Pro His Arg Leu Gly Arg Thr Pro Gly
1 5 10 15

Thr His His Met Pro Asp Leu Arg Cys Pro Gly Asp His Pro Pro Ala
20 25 30

Glu Glu Gly Arg Arg Ile Gln Arg Pro Ala Thr Val Pro Arg Leu Leu
35 40 45

Pro Val Thr Pro Arg Pro Gly Gly Ser Ala Met Thr Gly Thr Cys Arg
50 55 60

Cys Leu Gly Cys Leu Ser Pro Ser Gln Gly Pro Lys Lys Leu Gly Trp
65 70 75 80

Gly Arg Asn Lys Pro Tyr Trp Ser Val Lys Lys Leu
85 90

<210> 212
<211> 83
<212> PRT
<213> Homo sapien

<400> 212

Met His Pro Pro Gly Phe Leu Ser Phe Leu Gly Tyr Ser Pro Asn Arg
1 5 10 15

Asn Glu Pro Leu Thr Gly Asn Ser Asp Leu Pro Phe Trp Ala Val Ile
20 25 30

Leu Ile Gly Leu Ala Gly Leu Leu Gly Leu Ile Thr Cys Leu Ile Cys
35 40 45

Gly Val Leu Val Thr Thr Arg Arg Arg Lys Lys Glu Gly Glu Tyr Asn
50 55 60

Val Gln Gln Gln Cys Pro Gly Tyr Tyr Gln Ser His Leu Asp Leu Glu
65 70 75 80

Asp Leu Gln

<210> 213
<211> 225
<212> PRT
<213> Homo sapien

<400> 213

Met Ala Thr His His Thr Leu Trp Met Gly Leu Ala Leu Leu Gly Val
1 5 10 15

Leu Gly Asp Leu Gln Ala Ala Pro Glu Ala Gln Val Ser Val Gln Pro
20 25 30

Asn Phe Gln Gln Asp Lys Phe Leu Gly Arg Trp Phe Ser Ala Gly Leu
35 40 45

Ala Ser Asn Ser Ser Trp Leu Arg Glu Lys Lys Ala Ala Leu Ser Met
50 55 60

Cys Lys Ser Val Val Ala Pro Ala Thr Asp Gly Gly Leu Asn Leu Thr
65 70 75 80

Ser Thr Phe Leu Arg Lys Asn Gln Cys Glu Thr Arg Thr Met Leu Leu
85 90 95

Gln Pro Ala Gly Ser Leu Gly Ser Tyr Ser Tyr Arg Ser Pro Arg Glu
100 105 110

Trp Gly Leu His Arg Pro Pro Gly Pro Ser Leu Gly Ala Thr Leu Ala
115 120 125

Gly Thr Thr Leu Gly Gln Pro Pro Ala Ala Glu Ile His Gly Val Gly
130 135 140

Gly Asp Trp Gly Ser Thr Tyr Ser Val Ser Val Val Glu Thr Asp Tyr
145 150 155 160

Asp Gln Tyr Ala Leu Leu Tyr Ser Gln Gly Ser Lys Gly Pro Gly Glu
165 170 175

Asp Phe Arg Met Ala Thr Leu Tyr Ser Arg Thr Gln Thr Pro Arg Ala
180 185 190

Glu Leu Lys Glu Lys Phe Thr Ala Phe Cys Lys Ala Gln Gly Phe Thr
195 200 205

Glu Asp Thr Ile Val Phe Leu Pro Gln Thr Asp Lys Cys Met Thr Glu
210 215 220

Gln
225

<210> 214
<211> 349
<212> PRT
<213> Homo sapien

<400> 214

Arg Arg His Ser Ser Arg Ser Ser Cys Ser Gly Pro Pro Arg Pro Gly
1 5 10 15

His Leu Pro Arg Ser Pro Thr Pro Leu Ala Pro Gly Pro Gly His Pro
20 25 30

Leu Cys Cys Arg Arg Met Ala Thr His His Thr Leu Trp Met Gly Leu
35 40 45

Ala Leu Leu Gly Val Leu Gly Asp Leu Gln Ala Ala Pro Glu Ala Gln
50 55 60

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Val Ser Val Gln Pro Asn Phe Gln Gln Asp Lys Val Arg Gly Phe Pro
65                  70                  75                  80

Ala Ser Ser Pro Arg Ala Thr Gly Pro Cys Gln Gly Lys Gly Thr Phe
                85                  90                  95

Arg Leu Gly Leu Pro Pro Gly Arg Ser Glu Arg Ser Pro Ala Val Pro
            100                 105                 110

Gly Ser Ala Gly Gln Gly Leu Ser Gly Arg Ala Gly Arg Arg Leu Gly
        115                 120                 125

Ser Arg Pro Arg Arg Leu Pro Ala Arg Ser Pro Pro Trp Ala Pro Arg
    130                 135                 140

Pro Val Ser Pro Asp Gly Pro Arg Arg His Arg Ala Thr His Ala Pro
145                 150                 155                 160

Thr Pro Ala Arg His Val His Pro Cys Gly His Ala Thr Pro Arg Gly
                165                 170                 175

His Thr Ser Ala Arg Ser Thr Pro Gly Cys Gln Asp Thr Gly Gly Trp
            180                 185                 190

Gly Thr Gly Met Ala Thr Asn Thr Pro Cys Ala Val Gly Val Gly Arg
        195                 200                 205

Asp Ala His Arg Thr Asp Ser Arg Arg Arg Ala Leu Ser Pro Gly Ser
    210                 215                 220

Cys Ser Gly Lys Arg Arg Ser Ala Gly Pro Arg Ala Ala Arg Pro Ser
225                 230                 235                 240

Leu Ala Ser Arg Arg Thr Pro Ala Val Arg Arg Ala Glu Pro Lys Thr
                245                 250                 255

Arg Pro Asp Pro Arg Gln Glu Cys Asp Val Leu Cys Arg Pro Leu Tyr
            260                 265                 270

Gly Pro Gly Ala Gln Pro Gly His Arg Ile Gly Thr Gly Gly Gly Gly
        275                 280                 285

Ala Glu Ala Gly Trp Trp Ala Ala Cys Glu Val Pro Gly Ala Leu Val
    290                 295                 300

Gln Arg Gly Pro Arg Leu Gln Leu Glu Leu Ala Pro Gly Glu Glu Gly
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305 310 315 320

Gly Val Val His Val Gln Val Cys Gly Gly Pro Cys His Gly Trp Trp
325 330 335

Pro Gln Pro Asp Leu His Leu Pro Gln Glu Lys Pro Val
340 345

<210> 215
<211> 413
<212> PRT
<213> Homo sapien

<400> 215

Met Ala Thr His His Thr Leu Trp Met Gly Leu Ala Leu Leu Gly Val
1 5 10 15

Leu Gly Asp Leu Gln Ala Ala Pro Glu Ala Gln Val Ser Val Gln Pro
20 25 30

Asn Phe Gln Gln Asp Lys Val Arg Gly Phe Pro Ala Ser Ser Pro Arg
35 40 45

Ala Thr Gly Pro Cys Gln Gly Lys Gly Thr Phe Arg Leu Gly Leu Pro
50 55 60

Pro Gly Arg Ser Glu Arg Ser Pro Ala Val Pro Gly Ser Ala Gly Gln
65 70 75 80

Gly Leu Ser Gly Arg Ala Gly Arg Arg Leu Gly Ser Arg Pro Arg Arg
85 90 95

Leu Pro Ala Arg Ala Leu Pro Gly His Arg Val Pro Ser Pro Leu Met
100 105 110

Gly His Ala Asp Thr Gly Pro His Thr Arg Pro Arg Gln Pro Asp Thr
115 120 125

Ser Thr Pro Val Gly Thr Arg Pro Pro Glu Asp Thr Arg Ala His Val
130 135 140

Pro His Leu Gly Ala Arg Thr Arg Ala Gly Gly Ala Gln Gly Trp Arg
145 150 155 160

Gln Thr Leu Arg Ala Arg Trp Gly Leu Gly Gly Thr Arg Thr Ala Gln
165 170 175

Thr Ala Gly Asp Ala Arg Ser Arg Pro Gly Ala Ala Arg Gly Ser Ala
180 185 190

Gly Ala Arg Val Pro Ala Pro Arg Ala Pro Pro Trp Arg Arg Gly Glu
195 200 205

Pro Gln Arg Ser Ala Glu Leu Ser Arg Arg Pro Ala Pro Ile Pro Ala
210 215 220

Arg Asn Ala Thr Ser Ser Ala Ala Arg Cys Met Gly Gln Ala Leu Ser
225 230 235 240

Gln Gly Thr Glu Ser Gly Pro Gly Ala Glu Gly Pro Lys Leu Ala Gly
245 250 255

Gly Arg Arg Ala Arg Phe Leu Gly Arg Trp Phe Ser Ala Gly Leu Ala
260 265 270

Ser Asn Ser Ser Trp Leu Arg Glu Lys Lys Ala Ala Leu Ser Met Cys
275 280 285

Lys Ser Val Val Ala Pro Ala Thr Asp Gly Gly Leu Asn Leu Thr Ser
290 295 300

Thr Phe Leu Arg Lys Asn Gln Cys Glu Thr Arg Thr Met Leu Leu Gln
305 310 315 320

Pro Ala Gly Ser Leu Gly Ser Tyr Ser Tyr Arg Ser Pro His Trp Gly
325 330 335

Ser Thr Tyr Ser Val Ser Val Val Glu Thr Asp Tyr Asp Gln Tyr Ala
340 345 350

Leu Leu Tyr Ser Gln Gly Ser Lys Gly Pro Gly Glu Asp Phe Arg Met
355 360 365

Ala Thr Leu Tyr Ser Arg Thr Gln Thr Pro Arg Ala Glu Leu Lys Glu
370 375 380

Lys Phe Thr Ala Phe Cys Lys Ala Gln Gly Phe Thr Glu Asp Thr Ile
385 390 395 400

Val Phe Leu Pro Gln Thr Asp Lys Cys Met Thr Glu Gln
405 410

<210> 216
<211> 410
<212> PRT
<213> Homo sapien

<400> 216

Met Ala Thr His His Thr Leu Trp Met Gly Leu Ala Leu Leu Gly Val
1 5 10 15

Leu Gly Asp Leu Gln Ala Ala Pro Glu Ala Gln Val Ser Val Gln Pro
20 25 30

Asn Phe Gln Gln Asp Lys Val Arg Gly Phe Pro Ala Ser Ser Pro Arg
35 40 45

Ala Thr Gly Pro Cys Gln Gly Lys Gly Thr Phe Arg Leu Gly Leu Pro
50 55 60

Pro Gly Arg Ser Glu Arg Ser Pro Ala Val Pro Gly Ser Ala Gly Gln
65 70 75 80

Gly Leu Ser Gly Arg Ala Gly Arg Arg Leu Gly Ser Arg Pro Arg Arg
85 90 95

Leu Pro Ala Arg Ser Pro Pro Trp Ala Pro Arg Pro Val Ser Pro Asp
100 105 110

Gly Pro Arg Arg His Arg Ala Thr His Ala Pro Thr Pro Ala Arg His
115 120 125

Val His Pro Cys Gly His Ala Thr Pro Arg Gly His Thr Ser Ala Arg
130 135 140

Ser Thr Pro Gly Cys Gln Asp Thr Gly Gly Trp Gly Thr Gly Met Ala
145 150 155 160

Thr Asn Thr Pro Cys Ala Val Gly Val Gly Arg Asp Ala His Arg Thr
165 170 175

Asp Ser Arg Arg Arg Ala Leu Ser Pro Gly Ser Cys Ser Gly Lys Arg
180 185 190

Arg Ser Ala Gly Pro Arg Ala Ala Arg Pro Ser Leu Ala Ser Arg Arg
195 200 205

Thr Pro Ala Val Arg Arg Ala Glu Pro Lys Thr Arg Pro Asp Pro Arg
210 215 220

Gln Glu Cys Asp Val Leu Cys Arg Pro Leu Tyr Gly Pro Gly Ala Gln
225 230 235 240

Pro Gly His Arg Ile Gly Thr Gly Gly Gly Gly Ala Glu Ala Gly Trp
245 250 255

Trp Ala Ala Cys Glu Gly Glu Gly Leu Ser Ser Gly Gly Ala Trp Pro
260 265 270

Asp Gly Gly Ala Gly Cys Gln Gly Arg Gly Gln Leu Leu Gly Arg Arg
275 280 285

Cys Glu Gly Arg Gly His Leu Leu Gly Arg Gly Leu Arg Gly Gly Gly
290 295 300

Gln Phe Leu Gly Arg Gly Val Arg Gly Val Ala Ala Arg Gly Ile Gly
305 310 315 320

Arg Gly Gly Gly Ala Gly Leu Glu Thr Gly Gly Val Asp Gly Arg Gly
325 330 335

Ala Pro Ala Gly Arg Arg Arg Trp Val Arg Arg Val Leu Ala Asp Ala
340 345 350

Gly Gly Gly Arg Ser Pro Gln Phe Pro Gly Ala Leu Val Gln Arg Gly
355 360 365

Pro Arg Leu Gln Leu Glu Leu Ala Pro Gly Glu Glu Gly Gly Val Val
370 375 380

His Val Gln Val Cys Gly Gly Pro Cys His Gly Trp Trp Pro Gln Pro
385 390 395 400

Asp Leu His Leu Pro Gln Glu Lys Pro Val
405 410

<210> 217
<211> 135
<212> PRT
<213> Homo sapien

<400> 217

Met Ala Ala Gly Pro Met Ala Ala Glu Pro Cys Gly Pro His Ala Leu
1 5 10 15

Val Ala Leu Ala Gly Leu Val Thr Gly Ile Pro Thr His His Pro Arg
20 25 30

Val Tyr Asn Ile His Ser Arg Thr Val Thr Arg Tyr Pro Ala Asn Ser
35 40 45

Ile Val Val Val Gly Gly Cys Pro Val Cys Arg Val Gly Val Leu Glu
50 55 60

Asp Cys Phe Thr Phe Leu Gly Ile Phe Leu Ala Ile Ile Leu Phe Arg
65 70 75 80

Ile Gly Pro Ala Ala Ile Gly Gln Trp Gln Pro Pro Asn Gly Ser Arg
85 90 95

Thr Gln Thr Pro Arg Ala Glu Leu Lys Glu Lys Phe Thr Ala Phe Cys
100 105 110

Lys Ala Gln Gly Phe Thr Glu Asp Thr Ile Val Phe Leu Pro Gln Thr
115 120 125

Asp Lys Cys Met Thr Glu Gln
130 135

<210> 218
<211> 150
<212> PRT
<213> Homo sapien

<400> 218

Ala Leu Leu Glu Ala Trp Ala Arg Asp Arg Gly Val Ser Val Gln Val
1 5 10 15

Arg Thr Ser Leu Pro Gln Pro Leu His Glu Glu Pro Pro Pro Trp Gly
20 25 30

Thr Trp Arg Pro Gly Ala His Ser Val Pro Gly Pro Ser Ser Ser Gln
35 40 45

Asp Val Gly Leu Gln Pro Gly Gly Gly His Arg Val Glu Gly Ala His
50 55 60

Gly Gly Tyr Arg Gly Thr Asn His Thr Gly Leu Arg His Ser Leu Leu
65 70 75 80

Gly Val Asp Ser Leu Leu Leu Ala Glu Val Glu Lys Asp Pro Leu Phe
85 90 95

Val Ser Ser Ala Gln Gly Glu Val Gly Gly Asp Gly Gly Ser Val Gln
100 105 110

Phe Gly Gly Ser Val Lys Thr Ser Ser Ala Leu Arg Glu Glu Gln Glu
115 120 125

Ala Gln Trp Glu Asn Trp Pro Lys Ser Gly Val Leu Thr Thr Ala Pro
130 135 140

Gly Phe Phe Leu Gly Arg
145 150

<210> 219
<211> 224
<212> PRT
<213> Homo sapien

<400> 219

Met Ala Thr His His Thr Leu Trp Met Gly Leu Ala Leu Leu Gly Val
1 5 10 15

Leu Gly Asp Leu Gln Ala Ala Pro Glu Ala Gln Val Ser Val Gln Pro
20 25 30

Asn Phe Gln Gln Asp Lys Phe Leu Gly Arg Trp Phe Ser Ala Gly Leu
35 40 45

Ala Ser Asn Ser Ser Trp Leu Arg Glu Lys Lys Ala Ala Leu Ser Met
50 55 60

Cys Lys Ser Val Val Ala Pro Ala Thr Asp Gly Gly Leu Asn Leu Thr
65 70 75 80

Ser Thr Phe Leu Arg Lys Asn Gln Cys Glu Thr Arg Thr Met Leu Leu
85 90 95

Gln Pro Ala Gly Ser Leu Gly Ser Tyr Ser Tyr Arg Ser Pro Arg Glu
100 105 110

Trp Gly Leu His Arg Pro Pro Gly Pro Ser Leu Gly Ala Thr Leu Ala
115 120 125

Gly Thr Thr Leu Gly Gln Pro Pro Ala Ala Glu Ile His Gly Val Gly
130 135 140

Asp Trp Gly Ser Thr Tyr Ser Val Ser Val Val Glu Thr Asp Tyr Asp
145 150 155 160

Gln Tyr Ala Leu Leu Tyr Ser Gln Gly Ser Lys Gly Pro Gly Glu Asp
165 170 175

Phe Arg Met Ala Thr Leu Tyr Ser Arg Thr Gln Thr Pro Arg Ala Glu
180 185 190

Leu Lys Glu Lys Phe Thr Ala Phe Cys Lys Ala Gln Gly Phe Thr Glu
195 200 205

Asp Thr Ile Val Phe Leu Pro Gln Thr Asp Lys Cys Met Thr Glu Gln
210 215 220

<210> 220
<211> 481
<212> PRT
<213> Homo sapien

<400> 220

Met Ala Thr His His Thr Leu Trp Met Gly Leu Ala Leu Leu Gly Val
1 5 10 15

Leu Gly Asp Leu Gln Ala Ala Pro Glu Ala Gln Val Ser Val Gln Pro
20 25 30

Asn Phe Gln Gln Asp Lys Val Arg Gly Phe Pro Ala Ser Ser Pro Arg
35 40 45

Ala Thr Gly Pro Cys Gln Gly Lys Gly Thr Phe Arg Leu Gly Leu Pro
50 55 60

Pro Gly Arg Ser Glu Arg Ser Pro Ala Val Pro Gly Ser Ala Gly Gln
65 70 75 80

Gly Leu Ser Gly Arg Ala Gly Arg Arg Leu Gly Ser Arg Pro Arg Arg
85 90 95

Leu Pro Ala Arg Ser Pro Pro Trp Ala Pro Arg Pro Val Ser Pro Asp
100 105 110

Gly Pro Arg Arg His Arg Ala Thr His Ala Pro Thr Pro Ala Arg His
115 120 125

Val His Pro Cys Gly His Ala Thr Pro Arg Gly His Thr Ser Ala Arg
130 135 140

Ser Thr Pro Gly Cys Gln Asp Thr Gly Gly Trp Gly Thr Gly Met Ala
145 150 155 160

Thr Asn Thr Pro Cys Ala Val Gly Val Gly Arg Asp Ala His Arg Thr
165 170 175

Asp Ser Arg Arg Arg Ala Leu Ser Pro Gly Ser Cys Ser Gly Lys Arg
180 185 190

Arg Ser Ala Gly Pro Arg Ala Ala Arg Pro Ser Leu Ala Ser Arg Arg
195 200 205

Thr Pro Ala Val Arg Arg Ala Glu Pro Lys Thr Arg Pro Asp Pro Arg
210 215 220

Gln Glu Cys Asp Val Leu Cys Arg Pro Leu Tyr Gly Pro Gly Ala Gln
225 230 235 240

Pro Gly His Arg Ile Gly Thr Gly Gly Gly Gly Ala Glu Ala Gly Trp
245 250 255

Trp Ala Ala Cys Glu Gly Glu Gly Leu Ser Ser Gly Gly Ala Trp Pro
260 265 270

Asp Gly Gly Ala Gly Cys Gln Gly Arg Gly Gln Leu Leu Gly Arg Arg
275 280 285

Cys Glu Gly Arg Gly His Leu Leu Gly Arg Gly Leu Arg Gly Gly Gly
290 295 300

Gln Phe Leu Gly Arg Gly Val Arg Gly Val Ala Ala Arg Gly Ile Gly
305 310 315 320

Arg Gly Gly Gly Ala Gly Leu Glu Thr Gly Gly Val Asp Gly Arg Gly
325 330 335

Ala Pro Ala Gly Arg Arg Arg Trp Val Arg Arg Val Leu Ala Asp Ala
340 345 350

Gly Gly Gly Arg Ser Pro Gln Phe Leu Gly Arg Trp Phe Ser Ala Gly
355 360 365

Leu Ala Ser Asn Ser Ser Trp Leu Arg Glu Lys Lys Ala Ala Leu Ser
370 375 380

Met Cys Lys Ser Val Val Ala Pro Ala Thr Asp Gly Gly Leu Asn Leu
385 390 395 400

Thr Ser Thr Phe Leu Arg Lys Asn Gln Cys Glu Thr Arg Thr Met Leu
405 410 415

Leu Gln Pro Ala Gly Ser Leu Gly Ser Tyr Ser Tyr Arg Ser Pro Arg
420 425 430

Glu Trp Gly Leu His Arg Pro Pro Gly Pro Ser Leu Gly Ala Thr Leu
435 440 445

Ala Gly Thr Thr Leu Gly Gln Pro Pro Ala Ala Glu Ile His Gly Val
450 455 460

Gly Gly Asp Gly Cys Pro Thr Ser Val Arg Gly Lys Gly Gln Ala Trp
465 470 475 480

Ala

<210> 221
<211> 1088
<212> PRT
<213> Homo sapien

<400> 221

Met Asp Ile Tyr Asp Thr Gln Thr Leu Gly Val Val Val Phe Gly Gly
1 5 10 15

Phe Met Val Val Ser Ala Ile Gly Ile Phe Leu Val Ser Thr Phe Ser
20 25 30

Met Lys Glu Thr Ser Tyr Glu Glu Ala Leu Ala Asn Gln Arg Lys Glu
35 40 45

Met Ala Lys Thr His His Gln Lys Val Glu Lys Lys Lys Lys Glu Lys
50 55 60

Thr Val Glu Lys Lys Gly Lys Thr Lys Lys Lys Glu Glu Lys Pro Asn
65 70 75 80

Gly Lys Ile Pro Asp His Asp Pro Ala Pro Asn Val Thr Val Leu Leu
85 90 95

Arg Glu Pro Val Arg Ala Pro Ala Val Ala Val Ala Pro Thr Pro Val

100 105 110

Gln Pro Pro Ile Ile Val Ala Pro Val Ala Thr Val Pro Ala Met Pro
115 120 125

Gln Glu Lys Leu Ala Ser Ser Pro Lys Asp Lys Lys Lys Lys Glu Lys
130 135 140

Lys Val Ala Lys Val Glu Pro Ala Val Ser Ser Val Val Asn Ser Ile
145 150 155 160

Gln Val Leu Thr Ser Lys Ala Ala Ile Leu Glu Thr Ala Pro Lys Glu
165 170 175

Val Pro Met Val Val Val Pro Pro Val Gly Ala Lys Gly Asn Thr Pro
180 185 190

Ala Thr Gly Thr Thr Gln Gly Lys Lys Ala Glu Gly Thr Gln Asn Gln
195 200 205

Ser Lys Lys Ala Glu Gly Ala Pro Asn Gln Gly Arg Lys Ala Glu Gly
210 215 220

Thr Pro Asn Gln Gly Lys Lys Thr Glu Gly Thr Pro Asn Gln Gly Lys
225 230 235 240

Lys Ala Glu Gly Thr Pro Asn Gln Gly Lys Lys Ala Glu Gly Thr Pro
245 250 255

Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln Asn Gln Gly Lys Lys Val
260 265 270

Asp Thr Thr Pro Asn Gln Gly Lys Lys Val Glu Gly Ala Pro Thr Gln
275 280 285

Gly Arg Lys Ala Glu Gly Ala Gln Asn Gln Ala Lys Lys Val Glu Gly
290 295 300

Ala Gln Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln Asn Gln Gly Lys
305 310 315 320

Lys Gly Glu Gly Ala Gln Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln
325 330 335

Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln Asn Gln Gly Lys Lys Ala
340 345 350

Glu Gly Ala Gln Asn Gln Gly Gln Lys Gly Glu Gly Ala Gln Asn Gln
355 360 365

Gly Lys Lys Thr Glu Gly Ala Gln Gly Lys Lys Ala Glu Arg Ser Pro
370 375 380

Asn Gln Gly Lys Lys Gly Glu Gly Ala Pro Ile Gln Gly Lys Lys Ala
385 390 395 400

Asp Ser Val Ala Asn Gln Gly Thr Lys Val Glu Gly Ile Thr Asn Gln
405 410 415

Gly Lys Lys Ala Glu Gly Ser Pro Ser Glu Gly Lys Lys Ala Glu Gly
420 425 430

Ser Pro Asn Gln Gly Lys Lys Ala Asp Ala Ala Ala Asn Gln Gly Lys
435 440 445

Lys Thr Glu Ser Ala Ser Val Gln Gly Arg Asn Thr Asp Val Ala Gln
450 455 460

Ser Pro Glu Ala Pro Lys Gln Glu Ala Pro Ala Lys Lys Lys Ser Gly
465 470 475 480

Ser Lys Lys Lys Gly Glu Pro Gly Pro Pro Asp Ala Asp Gly Pro Leu
485 490 495

Tyr Leu Pro Tyr Lys Thr Leu Val Ser Thr Val Gly Ser Met Val Phe
500 505 510

Asn Glu Gly Glu Ala Gln Arg Leu Ile Glu Ile Leu Ser Glu Lys Ala
515 520 525

Gly Ile Ile Gln Asp Thr Trp His Lys Ala Thr Gln Lys Gly Asp Pro
530 535 540

Val Ala Ile Leu Lys Arg Gln Leu Glu Glu Lys Glu Lys Leu Leu Ala
545 550 555 560

Thr Glu Gln Glu Asp Ala Ala Val Ala Lys Ser Lys Leu Arg Glu Leu
565 570 575

Asn Lys Glu Met Ala Ala Glu Lys Ala Lys Ala Ala Ala Gly Glu Ala
580 585 590

Lys Val Lys Lys Gln Leu Val Ala Arg Glu Gln Glu Ile Thr Ala Val
595 600 605

Gln Ala Arg Met Gln Ala Ser Tyr Arg Glu His Val Lys Glu Val Gln
610 615 620

Gln Leu Gln Gly Lys Ile Arg Thr Leu Gln Glu Gln Leu Glu Asn Gly
625 630 635 640

Pro Asn Thr Gln Leu Ala Arg Leu Gln Gln Glu Asn Ser Ile Leu Arg
645 650 655

Asp Ala Leu Asn Gln Ala Thr Ser Gln Val Glu Ser Lys Gln Asn Ala
660 665 670

Glu Leu Ala Lys Leu Arg Gln Glu Leu Ser Lys Val Ser Lys Glu Leu
675 680 685

Val Glu Lys Ser Glu Ala Val Arg Gln Asp Glu Gln Gln Arg Lys Ala
690 695 700

Leu Glu Ala Lys Ala Ala Ala Phe Glu Lys Gln Val Leu Gln Leu Gln
705 710 715 720

Ala Ser His Arg Glu Ser Glu Glu Ala Leu Gln Lys Arg Leu Asp Glu
725 730 735

Val Ser Arg Glu Leu Cys His Thr Gln Ser Ser His Ala Ser Leu Arg
740 745 750

Ala Asp Ala Glu Lys Ala Gln Glu Gln Gln Gln Gln Met Ala Glu Leu
755 760 765

His Ser Lys Leu Gln Ser Ser Glu Ala Glu Val Arg Ser Lys Cys Glu
770 775 780

Glu Leu Ser Gly Leu His Gly Gln Leu Gln Glu Ala Arg Ala Glu Asn
785 790 795 800

Ser Gln Leu Thr Glu Arg Ile Arg Ser Ile Glu Ala Leu Leu Glu Ala
805 810 815

Gly Gln Ala Arg Asp Ala Gln Asp Val Gln Ala Ser Gln Ala Glu Ala
820 825 830

Asp Gln Gln Gln Thr Arg Leu Lys Glu Leu Glu Ser Gln Val Ser Gly
835 840 845

Leu Glu Lys Glu Ala Ile Glu Leu Arg Glu Ala Val Glu Gln Gln Lys
850 855 860

Val Lys Asn Asn Asp Leu Arg Glu Lys Asn Trp Lys Ala Met Glu Ala
865 870 875 880

Leu Ala Thr Ala Glu Gln Ala Cys Lys Glu Lys Leu His Ser Leu Thr
885 890 895

Gln Ala Lys Glu Glu Ser Glu Lys Gln Leu Cys Leu Ile Glu Ala Gln
900 905 910

Thr Met Glu Ala Leu Leu Ala Leu Leu Pro Glu Leu Ser Val Leu Ala
915 920 925

Gln Gln Asn Tyr Thr Glu Trp Leu Gln Asp Leu Lys Glu Lys Gly Pro
930 935 940

Thr Leu Leu Lys His Pro Pro Ala Pro Ala Glu Pro Ser Ser Asp Leu
945 950 955 960

Ala Ser Lys Leu Arg Glu Ala Glu Glu Thr Gln Ser Thr Leu Gln Ala
965 970 975

Glu Cys Asp Gln Tyr Arg Ser Ile Leu Ala Glu Thr Glu Gly Met Leu
980 985 990

Arg Asp Leu Gln Lys Ser Val Glu Glu Glu Glu Gln Val Trp Arg Ala
995 1000 1005

Lys Val Gly Ala Ala Glu Glu Glu Leu Gln Lys Val Tyr Ala Ala
1010 1015 1020

Leu Pro Ala Ser Arg Arg Arg Gly Ala His Glu Ala Gln Gly Arg
1025 1030 1035

Val Asp Arg Ile Val Ser Val Thr Cys Glu Thr Arg Val Ser Arg
1040 1045 1050

Trp Gly Phe Ser Thr Thr Pro Tyr Glu Ala Gln Leu Arg Asp Asp
1055 1060 1065

Ser Ser Val Arg Pro Pro Gly Gly Pro Arg Leu Gly Arg His Cys

1070 1075 1080

Gln Met Ala Pro Gly
1085

<210> 222
<211> 440
<212> PRT
<213> Homo sapien

<400> 222

Arg Val Gly Lys Ala Gly Gly Gly Asp Pro Gly Gly Gly Gly Arg Ser
1 5 10 15

Pro Ala Leu Arg Gln Lys Val Pro Arg Leu His Thr Arg Ala Arg Ser
20 25 30

Gln Arg Ala Ala Gly Ala Asp Gly Arg Arg Gly Gly Arg Arg Gln Gly
35 40 45

Arg Ser Val Tyr Ser Cys Ser Gly Ala Val Ser Trp Arg Arg Leu Gly
50 55 60

Arg Leu Leu Ser Pro Gly Ser Ala Ala Ala Ala Lys Ala Ala Ala Pro
65 70 75 80

Ala Leu Ser Leu Ser Leu Ser Arg Leu Trp Leu Gln Val Lys Gly Lys
85 90 95

Gln Ala Arg Met Asp Ile Tyr Asp Thr Gln Thr Leu Gly Val Val Val
100 105 110

Phe Gly Gly Phe Met Val Val Ser Ala Ile Gly Ile Phe Leu Val Ser
115 120 125

Thr Phe Ser Met Lys Glu Thr Ser Tyr Glu Glu Ala Leu Ala Asn Gln
130 135 140

Arg Lys Glu Met Ala Lys Thr His His Gln Lys Val Glu Lys Lys Lys
145 150 155 160

Lys Glu Lys Thr Val Glu Lys Lys Gly Lys Thr Lys Lys Lys Glu Glu
165 170 175

Lys Pro Asn Gly Lys Ile Pro Asp His Asp Pro Ala Pro Asn Val Thr
180 185 190

Val Leu Leu Arg Glu Pro Val Arg Ala Pro Ala Val Ala Val Ala Pro
195 200 205

Thr Pro Val Gln Pro Pro Ile Ile Val Ala Pro Val Ala Thr Val Pro
210 215 220

Ala Met Pro Gln Glu Lys Leu Ala Ser Ser Pro Lys Asp Lys Lys Lys
225 230 235 240

Lys Glu Lys Lys Val Ala Lys Val Glu Pro Ala Val Ser Ser Val Val
245 250 255

Asn Ser Ile Gln Val Leu Thr Ser Lys Ala Ala Ile Leu Glu Thr Ala
260 265 270

Pro Lys Glu Val Pro Met Val Val Val Pro Pro Val Gly Ala Lys Gly
275 280 285

Asn Thr Pro Ala Thr Gly Thr Thr Gln Gly Lys Lys Ala Glu Gly Thr
290 295 300

Gln Asn Gln Ser Lys Lys Ala Glu Gly Ala Pro Asn Gln Gly Arg Lys
305 310 315 320

Ala Glu Gly Thr Pro Asn Gln Gly Lys Lys Thr Glu Gly Thr Pro Asn
325 330 335

Gln Gly Lys Lys Ala Glu Gly Thr Pro Asn Gln Gly Lys Lys Ala Glu
340 345 350

Gly Thr Pro Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln Asn Gln Gly
355 360 365

Lys Lys Val Asp Thr Thr Pro Asn Gln Gly Lys Lys Val Glu Gly Ala
370 375 380

Pro Thr Gln Gly Arg Lys Ala Glu Gly Ala Gln Asn Gln Ala Lys Lys
385 390 395 400

Val Glu Gly Ala Gln Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln Asn
405 410 415

Gln Gly Lys Lys Gly Glu Gly Ala Gln Asn Gln Gly Lys Lys Ala Glu
420 425 430

Gly Ala Gln Asn Gln Pro Pro Met
435 440

<210> 223
<211> 521
<212> PRT
<213> Homo sapien

<400> 223

Met Asp Ile Tyr Asp Thr Gln Thr Leu Gly Val Val Val Phe Gly Gly
1 5 10 15

Phe Met Val Val Ser Ala Ile Gly Ile Phe Leu Val Ser Thr Phe Ser
20 25 30

Met Lys Glu Thr Ser Tyr Glu Glu Ala Leu Ala Asn Gln Arg Lys Glu
35 40 45

Met Ala Lys Thr His His Gln Lys Val Glu Lys Lys Lys Lys Glu Lys
50 55 60

Thr Val Glu Lys Lys Gly Lys Thr Lys Lys Lys Glu Glu Lys Pro Asn
65 70 75 80

Gly Lys Ile Pro Asp His Asp Pro Ala Pro Asn Val Thr Val Leu Leu
85 90 95

Arg Glu Pro Val Arg Ala Pro Ala Val Ala Val Ala Pro Thr Pro Val
100 105 110

Gln Pro Pro Ile Ile Val Ala Pro Val Ala Thr Val Pro Ala Met Pro
115 120 125

Gln Glu Lys Leu Ala Ser Ser Pro Lys Asp Lys Lys Lys Lys Glu Lys
130 135 140

Lys Val Ala Lys Val Glu Pro Ala Val Ser Ser Val Val Asn Ser Ile
145 150 155 160

Gln Val Leu Thr Ser Lys Ala Ala Ile Leu Glu Thr Ala Pro Lys Glu
165 170 175

Val Pro Met Val Val Val Pro Pro Val Gly Ala Lys Gly Asn Thr Pro
180 185 190

Ala Thr Gly Thr Thr Gln Gly Lys Lys Ala Glu Gly Thr Gln Asn Gln
195 200 205

Ser Lys Lys Ala Glu Gly Ala Pro Asn Gln Gly Arg Lys Ala Glu Gly
210 215 220

Thr Pro Asn Gln Gly Lys Lys Thr Glu Gly Thr Pro Asn Gln Gly Lys
225 230 235 240

Lys Ala Glu Gly Thr Pro Asn Gln Gly Lys Lys Ala Glu Gly Thr Pro
245 250 255

Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln Asn Gln Gly Lys Lys Val
260 265 270

Asp Thr Thr Pro Asn Gln Gly Lys Lys Val Glu Gly Ala Pro Thr Gln
275 280 285

Gly Arg Lys Ala Glu Gly Ala Gln Asn Gln Ala Lys Lys Val Glu Gly
290 295 300

Ala Gln Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln Asn Gln Gly Lys
305 310 315 320

Lys Gly Glu Gly Ala Gln Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln
325 330 335

Asn Gln Pro Pro Asp Val Thr Val Leu Leu Arg Glu Pro Val Arg Ala
340 345 350

Pro Ala Val Ala Val Ala Pro Thr Pro Val Gln Pro Pro Ile Ile Val
355 360 365

Ala Pro Val Ala Thr Val Pro Ala Met Pro Gln Glu Lys Leu Ala Ser
370 375 380

Ser Pro Lys Asp Lys Lys Lys Lys Glu Lys Asn Val Ala Lys Val Glu
385 390 395 400

Pro Ala Val Ser Ser Val Val Asn Ser Ile Gln Ser Ser His Phe Glu
405 410 415

Gly Cys Gln Val Gly Ser Met Val Phe Asn Glu Gly Glu Ala Gln Arg
420 425 430

Leu Ile Glu Ile Leu Ser Glu Lys Ala Gly Ile Ile Gln Asp Thr Trp
435 440 445

His Lys Ala Thr Gln Lys Gly Asp Pro Val Ala Ile Leu Lys Arg Gln
450 455 460

Leu Glu Glu Lys Glu Lys Leu Leu Ala Thr Glu Gln Glu Asp Ala Ala
465 470 475 480

Val Ala Lys Ser Lys Leu Arg Glu Leu Asn Lys Glu Met Ala Ala Glu
485 490 495

Lys Ala Lys Ala Ala Ala Gly Glu Ala Lys Val Lys Lys Gln Leu Val
500 505 510

Ala Arg Glu Gln Glu Ile Thr Ala Arg
515 520

<210> 224
<211> 165
<212> PRT
<213> Homo sapien

<400> 224

Gly Arg Ser Gln Arg Ser Ser Pro Cys Ser Ala Pro Leu Gln Gly Pro
1 5 10 15

Gly Ala Leu Gly Leu Arg Thr Gln Leu Leu Leu Pro Pro Trp Ser Ser
20 25 30

Thr Trp Glu Gln Val Ser Ser Trp Gly Val Trp Thr Gly Gly Ala Gly
35 40 45

Gly Arg Thr Gln Ala Gln Lys Leu Pro Ala Pro Thr Thr Gln Leu Leu
50 55 60

Ser Thr Ala Leu Glu Pro Thr Ser Gln Lys Pro Gly Val Gly Ala Gly
65 70 75 80

His Gly Gly Asp Pro Lys Leu Ser Pro His Lys Val Gln Gly Arg Ser
85 90 95

Glu Ala Gly Ala Gly Pro Gly Pro Lys Gln Gly His His Ser Ser Ser
100 105 110

Asp Ser Ser Ser Ser Ser Ser Asp Ser Asp Thr Asp Val Lys Ser His
115 120 125

Ala Ala Gly Ser Lys Gln His Glu Ser Ile Pro Gly Lys Ala Lys Lys

130 135 140

Pro Lys Val Lys Lys Lys Glu Lys Gly Lys Lys Glu Lys Gly Lys Lys
145 150 155 160

Lys Glu Ala Pro His
165

<210> 225
<211> 262
<212> PRT
<213> Homo sapien

<400> 225

Gly Arg Ser Gln Arg Ser Ser Pro Cys Ser Ala Pro Leu Gln Gly Pro
1 5 10 15

Gly Ala Leu Gly Leu Arg Thr Gln Leu Leu Leu Pro Pro Trp Ser Ser
20 25 30

Thr Trp Glu Gln Val Ser Ser Trp Gly Val Trp Thr Gly Gly Ala Gly
35 40 45

Gly Arg Thr Gln Ala Gln Lys Leu Pro Ala Pro Thr Thr Gln Leu Leu
50 55 60

Ser Thr Ala Leu Glu Pro Thr Ser Gln Lys Pro Gly Val Gly Ala Gly
65 70 75 80

His Gly Gly Asp Pro Lys Leu Ser Pro His Lys Val Gln Gly Arg Ser
85 90 95

Glu Ala Gly Ala Gly Pro Gly Pro Lys Val Ser Arg Leu Ile Thr Gly
100 105 110

Cys Gly Gly Ala Gly Arg Leu Gly Leu Pro Leu Thr Pro Gly Ser Cys
115 120 125

Leu Arg Pro Pro Thr Ser Gly Gly Trp Val Arg Gly Ala Ala Ser Leu
130 135 140

Pro His Leu His Pro Ala Arg Thr Pro Gln Leu Phe Arg Leu Gln Gln
145 150 155 160

Gln Leu Gln Arg Phe Gly His Gly Cys Glu Gly Lys Gly Leu Ser Pro
165 170 175

Ala Ser Pro Ser Thr Cys Pro Ala Pro Gln Arg Gly Val Pro Ala Leu
180 185 190

Gly Leu Ala Gly Arg Val Arg Gly Val Val Pro Leu Ser Arg Phe Gln
195 200 205

Pro Arg Thr Ile Ser Ser Leu Pro Ser Leu Pro Ser Ala Pro Gln Ser
210 215 220

His Ala Ala Gly Ser Lys Gln His Glu Ser Ile Pro Gly Lys Ala Lys
225 230 235 240

Lys Pro Lys Val Lys Lys Lys Glu Lys Gly Lys Lys Glu Lys Gly Lys
245 250 255

Lys Lys Glu Ala Pro His
260

<210> 226
<211> 231
<212> PRT
<213> Homo sapien

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<223> X=any amino acid

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<223> X=any amino acid

<400> 226

Ser Arg Asp Pro Asn Gly Trp Trp Arg Arg Leu Arg Val Ser Ala Glu
1 5 10 15

Leu Ala Met Ala Gln Leu Cys Gly Leu Arg Arg Ser Arg Ala Phe Leu
20 25 30

Ala Leu Leu Gly Ser Leu Leu Leu Ser Gly Val Leu Ala Ala Asp Arg
35 40 45

Glu Arg Ser Ile His Asp Phe Cys Leu Val Ser Lys Val Val Gly Arg
50 55 60

Cys Arg Ala Ser Met Pro Arg Trp Trp Tyr Asn Val Thr Asp Gly Ser

65 70 75 80

Cys Gln Leu Phe Val Tyr Gly Gly Cys Asp Gly Asn Ser Asn Asn Tyr
85 90 95

Leu Thr Lys Glu Glu Cys Leu Lys Lys Cys Ala Thr Val Thr Glu Asn
100 105 110

Ala Thr Gly Asp Leu Ala Thr Ser Arg Asn Ala Ala Asp Ser Ser Val
115 120 125

Pro Ser Ala Pro Arg Arg Gln Asp Ser Glu Asp His Ser Ser Asp Met
130 135 140

Phe Asn Tyr Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr Gly Pro Cys
145 150 155 160

Arg Ala Ser Phe Pro Arg Trp Tyr Phe Asp Val Glu Arg Asn Ser Cys
165 170 175

Asn Asn Phe Ile Tyr Gly Gly Cys Arg Gly Asn Lys Asn Ser Tyr Arg
180 185 190

Ser Glu Glu Ala Cys Met Leu Arg Cys Phe Gln Gly Asn Xaa Pro Ala
195 200 205

Leu Xaa Gln Gly Gly Pro Gly Gly Gly Pro Arg Gly Asp Pro Ser Gly
210 215 220

Arg Pro Gly Asp Arg Thr Gly
225 230

<210> 227
<211> 213
<212> PRT
<213> Homo sapien

<400> 227

Met Ala Gln Leu Cys Gly Leu Arg Arg Ser Arg Ala Phe Leu Ala Leu
1 5 10 15

Leu Gly Ser Leu Leu Leu Ser Gly Val Leu Ala Ala Asp Arg Glu Arg
20 25 30

Ser Ile His Asp Phe Cys Leu Val Ser Lys Val Val Gly Arg Cys Arg
35 40 45

Ala Ser Met Pro Arg Trp Trp Tyr Asn Val Thr Asp Gly Ser Cys Gln
50 55 60

Leu Phe Val Tyr Gly Gly Cys Asp Gly Asn Ser Asn Asn Tyr Leu Thr
65 70 75 80

Lys Glu Glu Cys Leu Lys Lys Cys Ala Thr Val Thr Glu Asn Ala Thr
85 90 95

Gly Asp Leu Ala Thr Ser Arg Asn Ala Ala Asp Ser Ser Val Pro Ser
100 105 110

Ala Pro Arg Arg Gln Asp Ser Glu Asp His Ser Ser Asp Met Phe Asn
115 120 125

Tyr Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr Gly Pro Cys Arg Ala
130 135 140

Ser Phe Pro Arg Trp Tyr Phe Asp Val Glu Arg Asn Ser Cys Asn Asn
145 150 155 160

Phe Ile Tyr Gly Gly Cys Arg Gly Asn Lys Asn Ser Tyr Arg Ser Glu
165 170 175

Glu Ala Cys Met Leu Arg Cys Phe Gln Arg Glu Leu Pro Trp Pro Trp
180 185 190

Ala Lys Gly Gly Arg Gly Ala Ala Arg Gly Gly Thr Pro Arg Gly Ala
195 200 205

Gln Gly Thr Glu Pro
210

<210> 228
<211> 242
<212> PRT
<213> Homo sapien

<400> 228

Met Ala Gln Leu Cys Gly Leu Arg Arg Ser Arg Ala Phe Leu Ala Leu
1 5 10 15

Leu Gly Ser Leu Leu Leu Ser Gly Val Leu Ala Ala Asp Arg Glu Arg
20 25 30

Ser Ile His Asp Phe Cys Leu Val Ser Lys Val Val Gly Arg Cys Arg

35 40 45

Ala Ser Met Pro Arg Trp Trp Tyr Asn Val Thr Asp Gly Ser Cys Gln
50 55 60

Leu Phe Val Tyr Gly Gly Cys Asp Gly Asn Ser Asn Asn Tyr Leu Thr
65 70 75 80

Lys Glu Glu Cys Leu Lys Lys Cys Ala Thr Val Thr Glu Asn Ala Thr
85 90 95

Gly Asp Leu Ala Thr Ser Arg Asn Ala Ala Asp Ser Ser Val Pro Ser
100 105 110

Ala Pro Arg Arg Gln Asp Ser Glu Asp His Ser Ser Asp Met Phe Asn
115 120 125

Tyr Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr Gly Pro Cys Arg Ala
130 135 140

Ser Phe Pro Arg Trp Tyr Phe Asp Val Glu Arg Asn Ser Cys Asn Asn
145 150 155 160

Phe Ile Tyr Gly Gly Cys Arg Gly Asn Lys Asn Ser Tyr Arg Ser Glu
165 170 175

Glu Ala Cys Met Leu Arg Cys Phe Arg Gln Gln Glu Asn Pro Pro Leu
180 185 190

Pro Leu Gly Ser Lys Gly Lys Trp Pro Leu Thr Leu Leu Leu Pro Ser
195 200 205

Ala Cys Leu Leu Pro Ser Leu Thr Glu Leu Ser Pro Ala Gln Leu Trp
210 215 220

Phe Thr Leu Ser Phe Thr Val Asn Ile Ile Leu Ala Glu Ser His Val
225 230 235 240

Ser Ala

<210> 229
<211> 53
<212> PRT
<213> Homo sapien

<400> 229

Arg Phe Trp Leu Ala Ile Gly Cys Trp Pro Ser Arg Gln Ser Arg Glu
1   5   10   15

Gln His Ile Ser Ser Arg Arg Lys Met Glu Ile Leu Lys Thr Glu Cys
            20   25   30

Gln Glu Lys Glu Ser Arg Thr Ile His Ser Met Arg Arg Lys Met Glu
        35   40   45

Lys Lys Asn Phe Ile
    50

<210> 230
<211> 43
<212> PRT
<213> Homo sapien

<400> 230

Met Asp Arg Pro Pro Gly Gln Val Pro Gly His Leu Gly Gln Cys Asp
1   5   10   15

Val Ser Gly Trp Gln Ser Asp Ala Gly Pro Ala Gly Ser Gln Glu Asn
            20   25   30

Ser Thr Leu Val Pro Glu Glu Arg Trp Lys Phe
        35   40

<210> 231
<211> 66
<212> PRT
<213> Homo sapien

<400> 231

Val Ala Ala Glu Val Pro Gly His Leu Gly Gln Cys Asp Val Ser Gly
1   5   10   15

Trp Gln Ser Asp Ala Gly Pro Ala Gly Ser Gln Glu Asn Ser Thr Leu
            20   25   30

Val Pro Glu Glu Arg Trp Glu Ile Leu Lys Thr Glu Cys Gln Glu Lys
        35   40   45

Glu Ser Arg Thr Ile His Ser Met Arg Arg Lys Met Glu Lys Lys Asn
    50   55   60

Phe Ile
65

<210> 232
<211> 34
<212> PRT
<213> Homo sapien

<400> 232

Met Asp Arg Ser Arg Pro Arg Tyr Leu Ala Ile Leu Gly Ser Val Thr
1 5 10 15

Phe Leu Ala Gly Asn Arg Met Leu Ala Gln Gln Ala Val Lys Arg Thr
20 25 30

Ala His

<210> 233
<211> 116
<212> PRT
<213> Homo sapien

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<223> X=any amino acid

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<223> X=any amino acid

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<223> X=any amino acid

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<222> (57)..(57)
<223> X=any amino acid

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<223> X=any amino acid

<220>
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<223> X=any amino acid

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<223> X=any amino acid

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<223> X=any amino acid

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<223> X=any amino acid

<220>
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<223> X=any amino acid

<220>
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<222> (97)..(97)
<223> X=any amino acid

<220>
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<222> (115)..(115)
<223> X=any amino acid

<400> 233

Met Val Xaa Xaa Arg Pro Ser Pro Leu Xaa Xaa Asp Leu Asn Ala Pro
1 5 10 15

Ser Asp Trp Asp Ser Arg Gly Lys Asp Ser Tyr Glu Thr Arg Xaa Leu
20 25 30

Asp Xaa Lys Ser Ala Glu Xaa Lys Xaa Lys Lys Xaa Ser Arg Leu Tyr
35 40 45

Lys Arg Lys Ala Asn Asp Glu Ser Xaa Glu Xaa Xaa Asp Val Ile Asp
50 55 60

Xaa Xaa Glu Leu Xaa Lys Xaa Ser Arg Glu Xaa Xaa Ser His Glu Xaa
65 70 75 80

Xaa Ser Xaa Glu Asp Met Leu Val Val Asp Ala Lys Ser Lys Glu Glu
85 90 95

Xaa Lys His Leu Lys Phe Arg Ile Ser His Glu Leu Asp Ser Ala Ser
100 105 110

Ser Glu Xaa Asn
115

<210> 234
<211> 122
<212> PRT
<213> Homo sapien

<220>
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<222> (9)..(10)
<223> X=any amino acid

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<223> X=any amino acid

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<223> X=any amino acid

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<223> X=any amino acid

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<223> X=any amino acid

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<223> X=any amino acid

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<223> X=any amino acid

<400> 234

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Met Glu Ser Glu Glu Leu Asn Gly Xaa Xaa Lys Ala Ile Pro Val Xaa
1               5                   10                  15

Xaa Asp Leu Asn Ala Pro Ser Asp Trp Asp Ser Arg Gly Lys Asp Ser
            20                  25                  30

Tyr Glu Thr Arg Xaa Leu Asp Xaa Lys Ser Ala Glu Xaa Lys Xaa Lys
        35                  40                  45

Lys Lys Ser Arg Leu Tyr Lys Arg Lys Ala Asn Asp Glu Ser Lys Glu
    50                  55                  60

Gln Ala Asp Val Ile Asp Arg Lys Glu Leu Ala Lys Asp Ser Arg Glu
65                  70                  75                  80

Ala Asn Ser His Glu Phe Xaa Ser Lys Glu Asp Met Leu Val Val Asp
                85                  90                  95

Ala Lys Ser Lys Glu Glu Glu Lys His Leu Lys Phe Arg Ile Ser His
            100                 105                 110

Glu Leu Asp Ser Ala Ser Ser Glu Phe Asn
        115                 120
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<210> 235

<211> 86
<212> PRT
<213> Homo sapien

<400> 235

Leu Ser Gly Leu Phe Arg Ser Leu Glu Val Ile Phe Val Ile Phe Phe
1 5 10 15

Leu Asn Tyr Phe Arg Glu Leu Gly Met Gln Met Phe Ser Val Arg Lys
20 25 30

Pro Leu Phe Thr Leu Trp Lys Leu Asn Lys Lys Cys Ile Cys Leu Arg
35 40 45

Asn Trp Arg Leu Leu Met Leu Gly Asn Thr Cys Asn Gly Ser Arg Gly
50 55 60

Asn Cys Val Ser Val Phe Gly Asn Glu Ile Tyr Gly Lys Pro Phe Phe
65 70 75 80

Lys Leu Val Met Leu Leu
85

<210> 236
<211> 30
<212> PRT
<213> Homo sapien

<400> 236

Lys Ser Gly Ile Asn Ala Glu Gly Pro Leu Arg Pro Gly Ala Ala Ile
1 5 10 15

Leu Gly Leu Leu Gly Leu Ala Ser Val Gly Asp Ser Arg Thr
20 25 30

<210> 237
<211> 125
<212> PRT
<213> Homo sapien

<220>
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<222> (70)..(70)
<223> X=any amino acid

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<223> X=any amino acid

<220>
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<222> (92)..(92)
<223> X=any amino acid

<400> 237

Gln Arg Leu Gln Arg Val Ala Gly Ile Thr Gly Thr Cys His His Thr
1 5 10 15

Gln Leu Ile Phe Ile Phe Leu Val Glu Thr Gly Phe His His Val Gly
20 25 30

Gln Ala Gly Phe Glu Leu Leu Ile Trp Trp Ser Ala Cys Leu Gly Leu
35 40 45

Pro Glu Cys Trp Asp Tyr Arg Arg Lys Pro Pro Arg Leu Ala Lys Lys
50 55 60

Ile Lys Ile Tyr Leu Xaa Tyr Val Leu Thr Ser Tyr Thr Gln Arg Ile
65 70 75 80

Leu Asp Phe Xaa Leu Lys Ile Ile Ile Lys Pro Xaa Ile Ser Pro Val
85 90 95

Glu Lys Glu Ile Leu Arg Phe Leu Cys Phe Phe Phe Gln His Asn Ser
100 105 110

Val Thr Tyr Gly Trp Glu Lys Ile Cys Arg Glu Ile Ile
115 120 125

<210> 238
<211> 104
<212> PRT
<213> Homo sapien

<400> 238

Thr Arg Thr Gln Arg Gly Thr Ile Gly Gln Asn Ile Ser His Thr His
1 5 10 15

Gln Arg His Thr Lys Pro Pro Thr His Ala Ile Thr Arg Pro Leu Ile
20 25 30

Arg Thr Leu Ala Glu Pro Asp Trp Lys Ser Thr Arg Ser Thr Lys Tyr
35 40 45

Ile Gly Asn Pro Pro His Arg Asn Pro Lys Leu Asp Lys Ala Lys Ile

50 55 60

Thr Ala Thr Thr Pro Ile Asn Lys Lys Pro Asn Thr Arg His Thr Arg
65 70 75 80

Asn Pro Pro Pro Asn Arg Arg Pro Met Pro Ile His Gln Gln Thr His
85 90 95

Thr Lys Asp Lys Lys Arg His Glu
100

<210> 239
<211> 61
<212> PRT
<213> Homo sapien

<400> 239

Met His Gln Gly Arg Glu His Ser Ala Gln Thr Ile Asp Ser Asp Tyr
1 5 10 15

Leu Leu Thr Val Cys Arg Arg His Ala Gly Gly Leu Lys Arg Gly Cys
20 25 30

Ile Leu Leu Pro Ser Leu Ala Gly Tyr Gly Ile Ser Ser Phe Pro Phe
35 40 45

Ile Gly Tyr Glu Val Tyr Ser Ser Ile Tyr Gln Asn Leu
50 55 60

<210> 240
<211> 193
<212> PRT
<213> Homo sapien

<400> 240

Ser Gly Gly Phe Thr Leu Arg Ser Thr Gly Ser Ala Ala Gly Arg Gly
1 5 10 15

Leu Arg Lys Leu Arg Pro Thr Leu Ser Arg Gly Ala Cys Asp Val Gly
20 25 30

Arg Ser Val Trp Lys Leu Arg Pro Ser His Cys Arg Val Gly Arg Gly
35 40 45

Ala Arg Gly Ile Phe His Ala Pro Pro Leu Cys Arg Leu Lys Cys Val
50 55 60

Gly Gly Lys Arg Trp Ala Gly Cys His Leu Ala Pro Pro Phe Ser Cys
65 70 75 80

Gly Val Gly Gln Ala Ala Ala Ser Ser Ser Cys Ser Ser His Arg Leu
85 90 95

His Ser Asp Pro Ser Pro Ala Ala Trp Ile Leu Leu Pro Arg Arg Gly
100 105 110

Ser Phe Ser Arg Asn Leu Arg Ala Arg Pro Gln Ser Val Pro Ala Ala
115 120 125

Ser Arg Arg Thr Arg Trp Leu Gln Ala Ser Leu Pro Gln Val Ser Trp
130 135 140

Leu Arg Glu Arg Gln Arg Glu Arg Gly Gly Lys Thr Arg Glu Gln Ala
145 150 155 160

Met Gly Gly Asp Gly Glu Ser Leu Leu Glu Gln Thr Arg Gly Arg Lys
165 170 175

Pro Thr Phe Leu His Ser Pro Ser Ile His Leu Trp Pro Tyr Val Phe
180 185 190

His

<210> 241
<211> 163
<212> PRT
<213> Homo sapien

<400> 241

Ser Gly Gly Phe Thr Leu Arg Ser Thr Gly Ser Ala Ala Gly Arg Gly
1 5 10 15

Leu Arg Lys Leu Arg Pro Thr Leu Ser Arg Gly Ala Cys Asp Val Gly
20 25 30

Arg Ser Val Trp Lys Leu Arg Pro Ser His Cys Arg Val Gly Arg Gly
35 40 45

Ala Arg Gly Ile Phe His Ala Pro Pro Leu Cys Arg Leu Lys Cys Val
50 55 60

Gly Gly Lys Arg Trp Ala Gly Cys His Leu Ala Pro Pro Phe Ser Cys
65 70 75 80

Gly Val Gly Gln Ala Ala Ala Ser Ser Ser Cys Ser Ser His Arg Leu
85 90 95

His Ser Asp Pro Ser Pro Ala Ala Trp Ile Leu Leu Pro Arg Arg Gly
100 105 110

Ser Phe Ser Arg Asn Leu Arg Ala Arg Pro Gln Ser Val Pro Ala Ala
115 120 125

Ser Arg Arg Thr Arg Trp Leu Gln Ala Ser Leu Thr Pro Gly Phe Leu
130 135 140

Ala Lys Arg Glu Thr Glu Gly Glu Arg Gly Glu Asp Glu Arg Thr Gly
145 150 155 160

Asn Gly Arg

<210> 242
<211> 227
<212> PRT
<213> Homo sapien

<220>
<221> MISC_FEATURE
<222> (3)..(4)
<223> X=any amino acid

<400> 242

Phe Phe Xaa Xaa Lys Glu Ala Gly Pro Pro Gly Leu Lys Thr His Ala
1 5 10 15

Gly Val Gly Pro Phe Trp Pro Val Gly Phe Leu Lys Pro Gln Trp Arg
20 25 30

Ala Leu Ser Ser Ser Phe Ser Gln Asn Pro Pro Gly Gly Leu Pro Leu
35 40 45

His Ser Phe Pro Asn Ser Gly Leu Pro Arg Arg His Arg Glu Thr Leu
50 55 60

Phe Gly Leu Pro Ser Lys Ser Arg Ala Met Leu Lys His Pro Trp Gly
65 70 75 80

Pro Gln Pro Phe Ser Pro Ser Val Pro Ala Lys Glu Pro Gln Gly Pro
85 90 95

Gly Gly His Gly Ala Arg Phe Arg Val Ala Lys Lys Ser Leu Val Pro
100 105 110

Asn Gln Gly Ala Ser Gln Gly Ala Leu Leu Lys Thr Leu Ser Pro Thr
115 120 125

Val Ile Trp Arg Gly Val Asn Ala Gly Gly Lys Pro Pro Arg Pro His
130 135 140

Gln Arg Gly Phe Gln Lys Glu Gln Pro Ala Arg Gly Pro Arg Leu Arg
145 150 155 160

Asn Asn Arg Arg Glu Thr Thr Gly Trp Ala Glu Pro Arg Val Lys Tyr
165 170 175

Pro Trp Leu Pro Ala Arg Asp Gly Asp Arg Arg Arg Ala Trp Cys Cys
180 185 190

Thr Trp Cys Tyr Trp Cys Ala Arg Lys Lys Tyr Pro Gly Leu Val Leu
195 200 205

Glu Val Pro Arg Asp Lys Leu Thr Ala Ala Gly Met Lys Thr Asp Glu
210 215 220

Gly Pro His
225

<210> 243
<211> 198
<212> PRT
<213> Homo sapien

<400> 243

Met Ala Cys Pro Phe Glu Leu Leu Phe Ser Lys Pro Pro Trp Gly Pro
1 5 10 15

Ser Pro Pro Leu Leu Pro Lys Phe Trp Ser Pro Gln Lys Thr Gln Gly
20 25 30

Asn Ile Val Trp Ser Ala Gln Gln Ile Lys Gly Asn Ala Gln Thr Pro
35 40 45

Met Gly Ala Pro Thr Leu Gln Pro Val Arg Ala Arg Gln Arg Thr Pro
50 55 60

Arg Pro Trp Gly Thr Trp Gly Ser Leu Gln Ser Cys Gln Lys Lys Pro
65 70 75 80

Cys Ala Lys Ser Gly Gly Leu Pro Arg Gly Ser Val Glu Asn Ile Val
85 90 95

Pro Tyr Gly Asp Met Glu Gly Gly Gln Cys Arg Gly Glu Ala Thr Lys
100 105 110

Ala Thr Ile Asn Gly Asp Ser Arg Arg Ser Ser Gln Gln Gly Ala His
115 120 125

Gly Tyr Glu Ile Thr Ala Glu Lys Pro Pro Val Gly Arg Asn Arg Val
130 135 140

Ser Asn Thr Leu Gly Cys Pro Gln Gly Thr Gly Thr Gly Ala Glu His
145 150 155 160

Gly Ala Val Leu Gly Val Thr Gly Val Leu Arg Lys Lys Tyr Pro Gly
165 170 175

Leu Val Leu Glu Val Pro Arg Asp Lys Leu Thr Ala Ala Gly Met Lys
180 185 190

Thr Asp Glu Gly Pro His
195

<210> 244
<211> 103
<212> PRT
<213> Homo sapien

<400> 244

Pro Lys Asp Ala Pro Glu Lys Leu Glu Asn Leu Phe Gln Val Gly Arg
1 5 10 15

Arg Val Gly Asp Thr Lys Ile Thr Leu Leu Tyr Arg Thr Leu Gln Leu
20 25 30

Ser Met Gln Glu Ile Pro Phe Ser Leu Ser Ala Pro Gly Lys Thr Gln
35 40 45

Gln Pro Thr Glu Ala Ile Gly Asp Ser Leu Ser Thr Arg Gly Met Phe
50 55 60

Ser Lys Gln Gly Val Pro Cys Leu Ser Asn Lys Cys Pro Pro Ser Leu
65 70 75 80

Leu Gly Phe Leu Phe Leu Gln Leu Val Val Ser Lys Pro Leu Pro Gly
85 90 95

Ile Val Lys Ala Leu Pro Lys
100

<210> 245
<211> 65
<212> PRT
<213> Homo sapien

<400> 245

Met Leu Pro Pro Ala Thr Ala Gln Leu Cys Leu Phe Asp Pro Arg Ala
1 5 10 15

Val Ala Gly Leu Tyr Ile Ser Leu Tyr Asp His Lys Leu Pro Ala Asn
20 25 30

Glu Ser Ile Cys Val Asp Asn Leu Thr Tyr Asn Ile Leu Ser Lys Ile
35 40 45

Met His Phe Arg Gln Thr Asp Ile Ser Leu Phe Ser Ile Tyr Ser Phe
50 55 60

Phe
65

<210> 246
<211> 103
<212> PRT
<213> Homo sapien

<400> 246

Pro Lys Asp Ala Pro Glu Lys Leu Glu Asn Leu Phe Gln Val Gly Arg
1 5 10 15

Arg Val Gly Asp Thr Lys Ile Thr Leu Leu Tyr Arg Thr Leu Gln Leu
20 25 30

Ser Met Gln Glu Ile Pro Phe Ser Leu Ser Ala Pro Gly Lys Thr Gln
35 40 45

Gln Pro Thr Glu Ala Ile Gly Asp Ser Leu Ser Thr Arg Gly Met Phe
50 55 60

Ser Lys Gln Gly Val Pro Cys Leu Ser Asn Lys Cys Pro Pro Ser Leu

65 70 75 80

Leu Gly Phe Leu Phe Leu Gln Leu Val Val Ser Lys Pro Leu Pro Gly
85 90 95

Ile Val Lys Ala Leu Pro Lys
100

<210> 247
<211> 27
<212> PRT
<213> Homo sapien

<400> 247

Met Lys Leu Leu Thr Pro Pro Gly Ala Asp Ser His Leu Asn Ser Thr
1 5 10 15

Pro Ser Lys Leu Arg Arg Ser Pro Ala Lys Asn
20 25

<210> 248
<211> 154
<212> PRT
<213> Homo sapien

<400> 248

Met Ala Ala Met Ala Ser Leu Gly Ala Leu Ala Leu Leu Leu Leu Ser
1 5 10 15

Ser Leu Ser Arg Cys Ser Ala Glu Ala Cys Leu Glu Pro Gln Ile Thr
20 25 30

Pro Ser Tyr Tyr Thr Thr Ser Asp Ala Val Ile Ser Thr Glu Thr Val
35 40 45

Phe Ile Val Glu Ile Ser Leu Thr Cys Lys Asn Arg Val Gln Asn Met
50 55 60

Ala Leu Tyr Ala Asp Val Gly Gly Lys Gln Phe Pro Val Thr Arg Gly
65 70 75 80

Gln Asp Val Gly Arg Tyr Gln Val Ser Trp Ser Leu Asp His Lys Ser
85 90 95

Ala His Ala Gly Thr Tyr Glu Val Arg Phe Phe Asp Glu Glu Ser Tyr
100 105 110

Ser Leu Leu Arg Lys Ala Gln Arg Asn Asn Glu Asp Ile Ser Ile Ile
115 120 125

Pro Pro Leu Phe Thr Val Ser Val Asp His Arg Val Ser Gly Leu Val
130 135 140

Pro Pro Pro Phe Trp Gly Cys Trp Ala Glu
145 150

<210> 249
<211> 176
<212> PRT
<213> Homo sapien

<400> 249

Leu Val Gln Ala Val Cys Gly Ser Glu Leu Arg Leu Ala Trp Pro Pro
1 5 10 15

Gly Leu Arg Val Ile Gly Pro Ser Val Ala Glu Ala Cys Leu Glu Pro
20 25 30

Gln Ile Thr Pro Ser Tyr Tyr Thr Thr Ser Asp Ala Val Ile Ser Thr
35 40 45

Glu Thr Val Phe Ile Val Glu Ile Ser Leu Thr Cys Lys Asn Arg Val
50 55 60

Gln Asn Met Ala Leu Tyr Ala Asp Val Gly Gly Lys Gln Phe Pro Val
65 70 75 80

Thr Arg Gly Gln Asp Val Gly Arg Tyr Gln Val Ser Trp Ser Leu Asp
85 90 95

His Lys Ser Ala His Ala Gly Thr Tyr Glu Val Arg Phe Phe Asp Glu
100 105 110

Glu Ser Tyr Ser Leu Leu Arg Lys Ala Gln Arg Asn Asn Glu Asp Ile
115 120 125

Ser Ile Ile Pro Pro Leu Phe Thr Val Ser Val Asp His Arg Gly Thr
130 135 140

Trp Asn Gly Pro Trp Val Ser Thr Glu Val Leu Ala Ala Ala Ile Gly
145 150 155 160

Leu Val Ile Tyr Tyr Leu Ala Phe Ser Ala Lys Ser His Ile Gln Ala
165 170 175

<210> 250
<211> 271
<212> PRT
<213> Homo sapien

<400> 250

Ala Thr Tyr Ala Ser Leu Phe Leu Val Cys Pro Ser Cys Ser Trp Glu
1 5 10 15

Leu Val Phe Phe Ser Ser Arg Gln Arg Arg Gly Asp Gly Gly Asp Gly
20 25 30

Ile Ser Arg Arg Pro Gly Ala Ala Pro Ala Val Gln Pro Leu Pro Leu
35 40 45

Leu Arg Lys Arg Trp Gly Gln Ser Ser Pro Ser Val Asn Trp Pro Gly
50 55 60

Ala Glu Thr Leu Ser Leu Ile Leu Lys Ala Pro Val His Cys Leu Pro
65 70 75 80

Ala Ala Pro Thr Pro Asp Val Ser Ala Glu Asp Ala Phe Ser Asn Ser
85 90 95

Ser Arg Pro Phe Val Ala Leu Asn Val Arg Leu Ala Trp Pro Pro Gly
100 105 110

Leu Arg Val Ile Gly Pro Ser Val Ala Glu Ala Cys Leu Glu Pro Gln
115 120 125

Ile Thr Pro Ser Tyr Tyr Thr Thr Ser Asp Ala Val Ile Ser Thr Glu
130 135 140

Thr Val Phe Ile Val Glu Ile Ser Leu Thr Cys Lys Asn Arg Val Gln
145 150 155 160

Asn Met Ala Leu Tyr Ala Asp Val Gly Gly Lys Gln Phe Pro Val Thr
165 170 175

Arg Gly Gln Asp Val Gly Arg Tyr Gln Val Ser Trp Ser Leu Asp His
180 185 190

Lys Ser Ala His Ala Gly Thr Tyr Glu Val Arg Phe Phe Asp Glu Glu
195 200 205

Ser Tyr Ser Leu Leu Arg Lys Ala Gln Arg Asn Asn Glu Asp Ile Ser
210 215 220

Ile Ile Pro Pro Leu Phe Thr Val Ser Val Asp His Arg Gly Thr Trp
225 230 235 240

Asn Gly Pro Trp Val Ser Thr Glu Val Leu Ala Ala Ala Ile Gly Leu
245 250 255

Val Ile Tyr Tyr Leu Ala Phe Ser Ala Lys Ser His Ile Gln Ala
260 265 270

<210> 251
<211> 268
<212> PRT
<213> Homo sapien

<400> 251

Met Lys Ser Val Ile Phe Gln Phe Gly Ile Lys Val Ser Phe Ser Val
1 5 10 15

Ala Ala Lys Cys Leu Val Met Lys Ala Glu Met Asn Gly Ser Lys Leu
20 25 30

Gly Arg Arg Ala Lys Pro Glu Gly Ala Leu Gln Asn Asn Asp Gly Leu
35 40 45

Tyr Asp Pro Asp Cys Asp Glu Ser Gly Leu Phe Lys Ala Lys Gln Cys
50 55 60

Asn Gly Thr Ser Met Cys Trp Cys Val Asn Thr Ala Gly Val Arg Arg
65 70 75 80

Thr Asp Lys Asp Thr Glu Ile Thr Cys Ser Glu Arg Val Arg Thr Tyr
85 90 95

Trp Ile Ile Ile Glu Leu Lys His Lys Ala Arg Glu Lys Pro Tyr Asp
100 105 110

Ser Lys Ser Leu Arg Thr Ala Leu Gln Lys Glu Ile Thr Thr Arg Tyr
115 120 125

Gln Leu Asp Pro Lys Phe Ile Thr Ser Ile Leu Tyr Glu Asn Asn Val
130 135 140

Ile Thr Ile Asp Leu Val Gln Asn Ser Ser Gln Lys Thr Gln Asn Asp
145 150 155 160

Val Asp Ile Ala Asp Val Ala Tyr Tyr Phe Glu Lys Asp Val Lys Gly
165 170 175

Glu Ser Leu Phe His Ser Lys Lys Met Asp Leu Thr Val Asn Gly Glu
180 185 190

Gln Leu Asp Leu Asp Pro Gly Gln Thr Leu Ile Tyr Tyr Val Asp Glu
195 200 205

Lys Ala Pro Glu Phe Ser Met Gln Gly Leu Lys Ala Gly Val Ile Ala
210 215 220

Val Ile Val Val Val Val Ile Ala Val Val Ala Gly Ile Val Val Leu
225 230 235 240

Val Ile Ser Arg Lys Lys Arg Met Ala Lys Tyr Glu Lys Ala Glu Ile
245 250 255

Lys Glu Met Gly Glu Met His Arg Glu Leu Asn Ala
260 265

<210> 252
<211> 342
<212> PRT
<213> Homo sapien

<400> 252

Met Glu Thr Lys His Leu Gly Arg Gly Gly Ala Gly Arg Ala Gly Pro
1 5 10 15

His Leu Trp Arg Gly Pro Arg Pro Asn Cys Ser Ala Gly Ala Gly Gly
20 25 30

Gly Glu Pro Thr His Ser Pro Asn Ser Arg Ala Val Thr His Gln Arg
35 40 45

Ala Pro Ala Ala Arg Glu Cys Val Cys Glu Asn Tyr Lys Leu Ala Val
50 55 60

Asn Cys Phe Val Asn Asn Asn Arg Gln Cys Gln Cys Thr Ser Val Gly
65 70 75 80

Ala Gln Asn Thr Val Ile Cys Ser Lys Leu Ala Ala Lys Cys Leu Val
85 90 95

Met Lys Ala Glu Met Asn Gly Ser Lys Leu Gly Arg Arg Ala Lys Pro
100 105 110

Glu Gly Ala Leu Gln Asn Asn Asp Gly Leu Tyr Asp Pro Asp Cys Asp
115 120 125

Glu Ser Gly Leu Phe Lys Ala Lys Gln Cys Asn Gly Thr Ser Met Cys
130 135 140

Trp Cys Val Asn Thr Ala Gly Val Arg Arg Thr Asp Lys Asp Thr Glu
145 150 155 160

Ile Thr Cys Ser Glu Arg Val Arg Thr Tyr Trp Ile Ile Ile Glu Leu
165 170 175

Lys His Lys Ala Arg Glu Lys Pro Tyr Asp Ser Lys Ser Leu Arg Thr
180 185 190

Ala Leu Gln Lys Glu Ile Thr Thr Arg Tyr Gln Leu Asp Pro Lys Phe
195 200 205

Ile Thr Ser Ile Leu Tyr Glu Asn Asn Val Ile Thr Ile Asp Leu Val
210 215 220

Gln Asn Ser Ser Gln Lys Thr Gln Asn Asp Val Asp Ile Ala Asp Val
225 230 235 240

Ala Tyr Tyr Phe Glu Lys Asp Val Lys Gly Glu Ser Leu Phe His Ser
245 250 255

Lys Lys Met Asp Leu Thr Val Asn Gly Glu Gln Leu Asp Leu Asp Pro
260 265 270

Gly Gln Thr Leu Ile Tyr Tyr Val Asp Glu Lys Ala Pro Glu Phe Ser
275 280 285

Met Gln Gly Leu Lys Ala Gly Val Ile Ala Val Ile Val Val Val Val
290 295 300

Ile Ala Val Val Ala Gly Ile Val Val Leu Val Ile Ser Arg Lys Lys
305 310 315 320

Arg Met Ala Lys Tyr Glu Lys Ala Glu Ile Lys Glu Met Gly Glu Met
325 330 335

His Arg Glu Leu Asn Ala

340

<210> 253
<211> 240
<212> PRT
<213> Homo sapien

<400> 253

Met Ala Pro Pro Gln Val Leu Ala Phe Gly Leu Leu Leu Ala Ala Ala
1   5   10   15

Thr Ala Thr Phe Ala Ala Ala Gln Glu Glu Cys Val Cys Glu Asn Tyr
            20   25   30

Lys Leu Ala Val Asn Cys Phe Val Asn Asn Asn Arg Gln Cys Gln Cys
        35   40   45

Thr Ser Val Gly Ala Gln Asn Thr Val Ile Cys Ser Lys Leu Ala Ala
    50   55   60

Lys Cys Leu Val Met Lys Ala Glu Met Asn Gly Ser Lys Leu Gly Arg
65   70   75   80

Arg Ala Lys Pro Glu Gly Ala Leu Gln Asn Asn Asp Gly Leu Tyr Asp
                85   90   95

Pro Asp Cys Asp Glu Ser Gly Leu Phe Lys Ala Lys Gln Cys Asn Gly
            100   105   110

Thr Ser Met Cys Trp Cys Val Asn Thr Ala Gly Val Arg Arg Thr Asp
        115   120   125

Lys Asp Thr Glu Ile Thr Cys Ser Glu Arg Val Arg Thr Tyr Trp Ile
    130   135   140

Ile Ile Glu Leu Lys His Lys Ala Arg Glu Lys Pro Tyr Asp Ser Lys
145   150   155   160

Ser Leu Arg Thr Ala Leu Gln Lys Glu Ile Thr Thr Arg Tyr Gln Leu
                165   170   175

Asp Pro Lys Phe Ile Thr Ser Ile Leu Tyr Glu Asn Asn Val Ile Thr
            180   185   190

Ile Asp Leu Val Gln Asn Ser Ser Gln Lys Thr Gln Asn Asp Val Asp
        195   200   205

Ile Ala Asp Val Ala Tyr Tyr Phe Glu Lys Asp Asp Val Ser Ile Ile
210 215 220

Phe Phe Ile Pro Val Phe Arg Asn Val Val Tyr His Ala Ser Met Asn
225 230 235 240

<210> 254
<211> 390
<212> PRT
<213> Homo sapien

<400> 254

Met Ala Pro Pro Gln Val Leu Ala Phe Gly Leu Leu Leu Ala Ala Ala
1 5 10 15

Thr Ala Thr Phe Ala Ala Ala Gln Glu Gly Glu Ala Arg Ile Gly Ala
20 25 30

Glu Leu Trp Ser Trp Ala Gly Leu Gly Gly Ser Gly Pro Arg Pro Ser
35 40 45

Ala Pro Glu Thr Gly Ile Ile Gly Arg Gly Pro Arg Gly Arg Ala Phe
50 55 60

Gln Arg Gly Asp Arg Thr Val Arg Pro Cys Ser Gly Ser Gly Pro Pro
65 70 75 80

Arg Gly Arg Lys Arg Arg Gly Pro Ser Arg Gly Ala Ala Ser Leu Arg
85 90 95

Ser Phe Ala Arg Leu Glu Cys Val Cys Glu Asn Tyr Lys Leu Ala Val
100 105 110

Asn Cys Phe Val Asn Asn Asn Arg Gln Cys Gln Cys Thr Ser Val Gly
115 120 125

Ala Gln Asn Thr Val Ile Cys Ser Lys Leu Ala Ala Lys Cys Leu Val
130 135 140

Met Lys Ala Glu Met Asn Gly Ser Lys Leu Gly Arg Arg Ala Lys Pro
145 150 155 160

Glu Gly Ala Leu Gln Asn Asn Asp Gly Leu Tyr Asp Pro Asp Cys Asp
165 170 175

Glu Ser Gly Leu Phe Lys Ala Lys Gln Cys Asn Gly Thr Ser Met Cys

180 185 190

Trp Cys Val Asn Thr Ala Gly Val Arg Arg Thr Asp Lys Asp Thr Glu
195 200 205

Ile Thr Cys Ser Glu Arg Val Arg Thr Tyr Trp Ile Ile Ile Glu Leu
210 215 220

Lys His Lys Ala Arg Glu Lys Pro Tyr Asp Ser Lys Ser Leu Arg Thr
225 230 235 240

Ala Leu Gln Lys Glu Ile Thr Thr Arg Tyr Gln Leu Asp Pro Lys Phe
245 250 255

Ile Thr Ser Ile Leu Tyr Glu Asn Asn Val Ile Thr Ile Asp Leu Val
260 265 270

Gln Asn Ser Ser Gln Lys Thr Gln Asn Asp Val Asp Ile Ala Asp Val
275 280 285

Ala Tyr Tyr Phe Glu Lys Asp Val Lys Gly Glu Ser Leu Phe His Ser
290 295 300

Lys Lys Met Asp Leu Thr Val Asn Gly Glu Gln Leu Asp Leu Asp Pro
305 310 315 320

Gly Gln Thr Leu Ile Tyr Tyr Val Asp Glu Lys Ala Pro Glu Phe Ser
325 330 335

Met Gln Gly Leu Lys Ala Gly Val Ile Ala Val Ile Val Val Val Val
340 345 350

Ile Ala Val Val Ala Gly Ile Val Val Leu Val Ile Ser Arg Lys Lys
355 360 365

Arg Met Ala Lys Tyr Glu Lys Ala Glu Ile Lys Glu Met Gly Glu Met
370 375 380

His Arg Glu Leu Asn Ala
385 390

<210> 255
<211> 314
<212> PRT
<213> Homo sapien

<400> 255

Met Ala Pro Pro Gln Val Leu Ala Phe Gly Leu Leu Leu Ala Ala Ala
1 5 10 15

Thr Ala Thr Phe Ala Ala Ala Gln Glu Glu Cys Val Cys Glu Asn Tyr
20 25 30

Lys Leu Ala Val Asn Cys Phe Val Asn Asn Asn Arg Gln Cys Gln Cys
35 40 45

Thr Ser Val Gly Ala Gln Asn Thr Val Ile Cys Ser Lys Leu Ala Ala
50 55 60

Lys Cys Leu Val Met Lys Ala Glu Met Asn Gly Ser Lys Leu Gly Arg
65 70 75 80

Arg Ala Lys Pro Glu Gly Ala Leu Gln Asn Asn Asp Gly Leu Tyr Asp
85 90 95

Pro Asp Cys Asp Glu Ser Gly Leu Phe Lys Ala Lys Gln Cys Asn Gly
100 105 110

Thr Ser Thr Cys Trp Cys Val Asn Thr Ala Gly Val Arg Arg Thr Asp
115 120 125

Lys Asp Thr Glu Ile Thr Cys Ser Glu Arg Val Arg Thr Tyr Trp Ile
130 135 140

Ile Ile Glu Leu Lys His Lys Ala Arg Glu Lys Pro Tyr Asp Ser Lys
145 150 155 160

Ser Leu Arg Thr Ala Leu Gln Lys Glu Ile Thr Thr Arg Tyr Gln Leu
165 170 175

Asp Pro Lys Phe Ile Thr Ser Ile Leu Tyr Glu Asn Asn Val Ile Thr
180 185 190

Ile Asp Leu Val Gln Asn Ser Ser Gln Lys Thr Gln Asn Asp Val Asp
195 200 205

Ile Ala Asp Val Ala Tyr Tyr Phe Glu Lys Asp Val Lys Gly Glu Ser
210 215 220

Leu Phe His Ser Lys Lys Met Asp Leu Thr Val Asn Gly Glu Gln Leu
225 230 235 240

Asp Leu Asp Pro Gly Gln Thr Leu Ile Tyr Tyr Val Asp Glu Lys Ala
245 250 255

Pro Glu Phe Ser Met Gln Gly Leu Lys Ala Gly Val Ile Ala Val Ile
260 265 270

Val Val Val Val Ile Ala Val Val Ala Gly Ile Val Val Leu Val Ile
275 280 285

Ser Arg Lys Lys Arg Met Ala Lys Tyr Glu Lys Ala Glu Ile Lys Glu
290 295 300

Met Gly Glu Met His Arg Glu Leu Asn Ala
305 310

<210> 256
<211> 122
<212> PRT
<213> Homo sapien

<400> 256

Gln Asn Leu Thr Cys Ala Glu Asn Lys Met Arg Leu Ala Trp Leu Tyr
1 5 10 15

Leu Phe Phe Leu Phe Cys Phe Gly Phe Phe Phe Phe Phe Gly Leu Thr
20 25 30

Gln Asp Leu Lys Thr Gly Thr Val Lys Val Thr Ala Val Gly Trp Ser
35 40 45

Glu His Pro Pro Lys Phe Thr Met Trp Pro Arg Thr Leu Ile Ala His
50 55 60

Cys Cys Phe Phe Asn Ser His Ser Lys Tyr Glu Met Arg Cys Tyr Arg
65 70 75 80

Lys Ser Leu Ala Ile Leu Lys Ala Thr Pro Leu Leu Ser Lys Glu Asn
85 90 95

Gly Pro Val Leu Ser Gln Val His Thr Gly Glu Val Ile Ala Leu Leu
100 105 110

Ser Cys Lys Leu Cys Asn Ala Lys Phe Phe
115 120

<210> 257
<211> 48

<212> PRT
<213> Homo sapien

<400> 257

Ala Leu Ser Ser Gly Arg Pro Gly Arg Tyr Ser Val Trp Ile Gly Gly
1 5 10 15

Ser Ile Leu Ala Ser Leu Ser Thr Phe Gln Gln Met Trp Ile Ser Lys
20 25 30

Gln Glu Tyr Asp Glu Ser Gly Pro Ser Ile Val His Arg Lys Cys Phe
35 40 45

<210> 258
<211> 596
<212> PRT
<213> Homo sapien

<400> 258

Met Asn Arg Thr Trp Pro Arg Arg Ile Trp Gly Ser Ser Gln Asp Glu
1 5 10 15

Ala Glu Leu Ile Arg Glu Asp Ile Gln Gly Ala Leu His Asn Tyr Arg
20 25 30

Ser Gly Arg Gly Glu Arg Arg Ala Ala Ala Leu Arg Ala Thr Gln Glu
35 40 45

Glu Leu Gln Arg Asp Arg Ser Pro Ala Ala Glu Thr Pro Pro Leu Gln
50 55 60

Arg Arg Pro Ser Val Arg Ala Val Ile Ser Thr Val Glu Arg Gly Ala
65 70 75 80

Gly Arg Gly Arg Pro Gln Ala Lys Pro Ile Pro Glu Ala Glu Glu Ala
85 90 95

Gln Arg Pro Glu Pro Val Gly Thr Ser Ser Asn Ala Asp Ser Ala Ser
100 105 110

Pro Asp Leu Gly Pro Arg Gly Pro Asp Leu Ala Val Leu Gln Ala Glu
115 120 125

Arg Glu Val Asp Ile Leu Asn His Val Phe Asp Asp Val Glu Ser Phe
130 135 140

Val Ser Arg Leu Gln Lys Ser Ala Glu Ala Ala Arg Val Leu Glu His

145 150 155 160

Arg Glu Arg Gly Arg Arg Ser Arg Arg Arg Ala Ala Gly Glu Gly Leu
165 170 175

Leu Thr Leu Arg Ala Lys Pro Pro Ser Glu Ala Glu Tyr Thr Asp Val
180 185 190

Leu Gln Lys Ile Lys Tyr Ala Phe Ser Leu Leu Ala Arg Leu Arg Gly
195 200 205

Asn Ile Ala Asp Pro Ser Ser Pro Glu Leu Leu His Phe Leu Phe Gly
210 215 220

Pro Leu Gln Met Ile Val Asn Thr Ser Gly Gly Pro Glu Phe Ala Ser
225 230 235 240

Ser Val Arg Arg Pro His Leu Thr Ser Asp Ala Val Ala Leu Leu Arg
245 250 255

Asp Asn Val Thr Pro Arg Glu Asn Glu Leu Trp Thr Ser Leu Gly Asp
260 265 270

Ser Trp Thr Arg Pro Gly Leu Glu Leu Ser Pro Glu Glu Gly Pro Pro
275 280 285

Tyr Arg Pro Glu Phe Phe Ser Gly Trp Glu Pro Pro Val Thr Asp Pro
290 295 300

Gln Ser Arg Ala Trp Glu Asp Pro Val Glu Lys Gln Leu Gln His Glu
305 310 315 320

Arg Arg Arg Arg Gln Gln Ser Ala Pro Gln Val Ala Val Asn Gly His
325 330 335

Arg Asp Leu Glu Pro Glu Ser Glu Pro Gln Leu Glu Ser Glu Thr Ala
340 345 350

Gly Lys Trp Val Leu Cys Asn Tyr Asp Phe Gln Ala Arg Asn Ser Ser
355 360 365

Glu Leu Ser Val Lys Gln Arg Asp Val Leu Glu Val Leu Asp Asp Ser
370 375 380

Arg Lys Trp Trp Lys Val Arg Asp Pro Ala Gly Gln Glu Gly Tyr Val
385 390 395 400

Pro Tyr Asn Ile Leu Thr Pro Tyr Pro Gly Pro Arg Leu His His Ser
405 410 415

Gln Ser Pro Ala Arg Ser Leu Asn Ser Thr Pro Pro Pro Pro Pro Ala
420 425 430

Pro Ala Pro Ala Pro Pro Pro Ala Leu Ala Arg Pro Arg Trp Asp Arg
435 440 445

Pro Arg Trp Asp Ser Cys Asp Ser Leu Asn Gly Leu Asp Pro Ser Glu
450 455 460

Lys Glu Lys Phe Ser Gln Met Leu Ile Val Asn Glu Glu Leu Gln Ala
465 470 475 480

Arg Leu Ala Gln Gly Arg Ser Gly Pro Ser Arg Ala Val Pro Gly Pro
485 490 495

Arg Ala Pro Glu Pro Gln Leu Ser Pro Gly Ser Asp Ala Ser Glu Val
500 505 510

Arg Ala Trp Leu Gln Ala Lys Gly Phe Ser Ser Gly Thr Val Asp Ala
515 520 525

Leu Gly Val Leu Thr Gly Ala Gln Leu Phe Ser Leu Gln Arg Glu Glu
530 535 540

Leu Arg Ala Val Ser Pro Glu Glu Gly Ala Arg Val Tyr Ser Gln Val
545 550 555 560

Thr Val Gln Arg Ser Leu Leu Glu Asp Lys Glu Lys Val Ser Glu Leu
565 570 575

Glu Ala Val Met Glu Lys Gln Lys Lys Lys Val Glu Gly Glu Val Glu
580 585 590

Met Glu Val Ile
595

<210> 259
<211> 408
<212> PRT
<213> Homo sapien

<400> 259

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Asp Leu Phe Gln Met Ser Pro Leu Ser Pro Gly Ser Pro Leu Pro Pro
1               5                   10                  15

Leu Ala Arg Ala Asp Leu Thr Ala Ile Leu Thr Gly Cys Pro Pro Leu
            20                  25                  30

Ser Ala Cys Leu Val Leu Ala Pro Arg Pro His Arg Arg Ala Arg Leu
        35                  40                  45

Leu Pro Ser Glu Gly Leu Leu Thr Leu Arg Ala Lys Pro Pro Ser Glu
    50                  55                  60

Ala Glu Tyr Thr Asp Val Leu Gln Lys Ile Lys Tyr Ala Phe Ser Leu
65                  70                  75                  80

Leu Ala Arg Leu Arg Gly Asn Ile Ala Asp Pro Ser Ser Pro Glu Leu
                85                  90                  95

Leu His Phe Leu Phe Gly Pro Leu Gln Met Ile Val Asn Thr Ser Gly
            100                 105                 110

Gly Pro Glu Phe Ala Ser Ser Val Arg Arg Pro His Leu Thr Ser Asp
        115                 120                 125

Ala Val Ala Leu Leu Arg Asp Asn Val Thr Pro Arg Glu Asn Glu Leu
    130                 135                 140

Trp Thr Ser Leu Gly Asp Ser Trp Thr Arg Pro Gly Leu Glu Leu Ser
145                 150                 155                 160

Pro Glu Glu Gly Pro Pro Tyr Arg Pro Glu Phe Phe Ser Gly Trp Glu
                165                 170                 175

Pro Pro Val Thr Asp Pro Gln Ser Arg Ala Trp Glu Asp Pro Val Glu
            180                 185                 190

Lys Gln Leu Gln His Glu Arg Arg Arg Arg Gln Gln Ser Ala Pro Gln
        195                 200                 205

Val Ala Val Asn Gly His Arg Asp Leu Glu Pro Glu Ser Glu Pro Gln
    210                 215                 220

Leu Glu Ser Glu Thr Ala Gly Lys Trp Val Leu Cys Asn Tyr Asp Phe
225                 230                 235                 240

Gln Ala Arg Asn Ser Ser Glu Leu Ser Val Lys Gln Arg Asp Val Leu
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245 250 255

Glu Val Leu Asp Asp Ser Arg Lys Trp Trp Lys Val Arg Asp Pro Ala
260 265 270

Gly Gln Glu Gly Tyr Val Pro Tyr Asn Ile Leu Thr Pro Tyr Pro Gly
275 280 285

Pro Arg Leu His His Ser Gln Ser Pro Ala Arg Ser Leu Asn Ser Thr
290 295 300

Pro Pro Pro Pro Pro Ala Pro Ala Pro Ala Pro Pro Pro Ala Leu Ala
305 310 315 320

Arg Pro Arg Trp Asp Arg Pro Arg Trp Asp Ser Cys Asp Ser Leu Asn
325 330 335

Gly Leu Asp Pro Ser Glu Lys Glu Lys Phe Ser Gln Met Leu Ile Val
340 345 350

Asn Glu Glu Leu Gln Ala Arg Leu Ala Gln Gly Arg Ser Gly Pro Ser
355 360 365

Arg Ala Val Pro Gly Pro Arg Ala Pro Glu Pro Gln Leu Ser Pro Gly
370 375 380

Ser Asp Ala Ser Glu Val Arg Ala Trp Leu Gln Ala Lys Gly Phe Ser
385 390 395 400

Ser Gly Arg Arg Ser Cys Gly Arg
405

<210> 260
<211> 470
<212> PRT
<213> Homo sapien

<400> 260

Met Ser Pro Leu Ser Pro Gly Ser Pro Leu Pro Pro Leu Ala Arg Ala
1 5 10 15

Asp Leu Thr Ala Ile Leu Thr Gly Cys Pro Pro Leu Ser Ala Cys Leu
20 25 30

Val Leu Ala Pro Arg Pro His Arg Arg Ala Arg Leu Leu Pro Ser Glu
35 40 45

Gly Leu Leu Thr Leu Arg Ala Lys Pro Pro Ser Glu Ala Glu Tyr Thr
50 55 60

Asp Val Leu Gln Lys Ile Lys Tyr Ala Phe Ser Leu Leu Ala Arg Leu
65 70 75 80

Arg Gly Asn Ile Ala Asp Pro Ser Ser Pro Glu Leu Leu His Phe Leu
85 90 95

Phe Gly Pro Leu Gln Met Ile Val Asn Thr Ser Gly Gly Pro Glu Phe
100 105 110

Ala Ser Ser Val Arg Arg Pro His Leu Thr Ser Asp Ala Val Ala Leu
115 120 125

Leu Arg Asp Asn Val Thr Pro Arg Glu Asn Glu Leu Trp Thr Ser Leu
130 135 140

Gly Asp Ser Trp Thr Arg Pro Gly Leu Glu Leu Ser Pro Glu Glu Gly
145 150 155 160

Pro Pro Tyr Arg Pro Glu Phe Phe Ser Gly Trp Glu Pro Pro Val Thr
165 170 175

Asp Pro Gln Ser Arg Ala Trp Glu Asp Pro Val Glu Lys Gln Leu Gln
180 185 190

His Glu Arg Arg Arg Arg Gln Gln Ser Ala Pro Gln Val Ala Val Asn
195 200 205

Gly His Arg Asp Leu Glu Pro Glu Ser Glu Pro Gln Leu Glu Ser Glu
210 215 220

Thr Ala Gly Lys Trp Val Leu Cys Asn Tyr Asp Phe Gln Ala Arg Asn
225 230 235 240

Ser Ser Glu Leu Ser Val Lys Gln Arg Asp Val Leu Glu Val Leu Asp
245 250 255

Asp Ser Arg Lys Trp Trp Lys Val Arg Asp Pro Ala Gly Gln Glu Gly
260 265 270

Tyr Val Pro Tyr Asn Ile Leu Thr Pro Tyr Pro Gly Pro Arg Leu His
275 280 285

His Ser Gln Ser Pro Ala Arg Ser Leu Asn Ser Thr Pro Pro Pro Pro
290 295 300

Pro Ala Pro Ala Pro Ala Pro Pro Pro Ala Leu Ala Arg Pro Arg Trp
305 310 315 320

Asp Arg Pro Arg Trp Asp Ser Cys Asp Ser Leu Asn Gly Leu Asp Pro
325 330 335

Ser Glu Lys Glu Lys Phe Ser Gln Met Leu Ile Val Asn Glu Glu Leu
340 345 350

Gln Ala Arg Leu Ala Gln Gly Arg Ser Gly Pro Ser Arg Ala Val Pro
355 360 365

Gly Pro Arg Ala Pro Glu Pro Gln Leu Ser Pro Gly Ser Asp Ala Ser
370 375 380

Glu Val Arg Ala Trp Leu Gln Ala Lys Gly Phe Ser Ser Gly Thr Val
385 390 395 400

Asp Ala Leu Gly Val Leu Thr Gly Ala Gln Leu Phe Ser Leu Gln Lys
405 410 415

Glu Glu Leu Arg Ala Val Ser Pro Glu Glu Gly Ala Arg Val Tyr Ser
420 425 430

Gln Val Thr Val Gln Arg Ser Leu Leu Glu Asp Lys Glu Lys Val Ser
435 440 445

Glu Leu Glu Ala Val Met Glu Lys Gln Lys Lys Lys Val Glu Gly Glu
450 455 460

Val Glu Met Glu Val Ile
465 470

<210> 261
<211> 474
<212> PRT
<213> Homo sapien

<400> 261

Asp Leu Phe Gln Met Ser Pro Leu Ser Pro Gly Ser Pro Leu Pro Pro
1 5 10 15

Leu Ala Arg Ala Asp Leu Thr Ala Ile Leu Thr Gly Cys Pro Pro Leu
20 25 30

Ser Ala Cys Leu Val Leu Ala Pro Arg Pro His Arg Arg Ala Arg Leu
35 40 45

Leu Pro Ser Glu Gly Leu Leu Thr Leu Arg Ala Lys Pro Pro Ser Glu
50 55 60

Ala Glu Tyr Thr Asp Val Leu Gln Lys Ile Lys Tyr Ala Phe Ser Leu
65 70 75 80

Leu Ala Arg Leu Arg Gly Asn Ile Ala Asp Pro Ser Ser Pro Glu Leu
85 90 95

Leu His Phe Leu Phe Gly Pro Leu Gln Met Ile Val Asn Thr Ser Gly
100 105 110

Gly Pro Glu Phe Ala Ser Ser Val Arg Arg Pro His Leu Thr Ser Asp
115 120 125

Ala Val Ala Leu Leu Arg Asp Asn Val Thr Pro Arg Glu Asn Glu Leu
130 135 140

Trp Thr Ser Leu Gly Asp Ser Trp Thr Arg Pro Gly Leu Glu Leu Ser
145 150 155 160

Pro Glu Glu Gly Pro Pro Tyr Arg Pro Glu Phe Phe Ser Gly Trp Glu
165 170 175

Pro Pro Val Thr Asp Pro Gln Ser Arg Ala Trp Glu Asp Pro Val Glu
180 185 190

Lys Gln Leu Gln His Glu Arg Arg Arg Arg Gln Gln Ser Ala Pro Gln
195 200 205

Val Ala Val Asn Gly His Arg Asp Leu Glu Pro Glu Ser Glu Pro Gln
210 215 220

Leu Glu Ser Glu Thr Ala Gly Lys Trp Val Leu Cys Asn Tyr Asp Phe
225 230 235 240

Gln Ala Arg Asn Ser Ser Glu Leu Ser Val Lys Gln Arg Asp Val Leu
245 250 255

Glu Val Leu Asp Asp Ser Arg Lys Trp Trp Lys Val Arg Asp Pro Ala
260 265 270

Gly Gln Glu Gly Tyr Val Pro Tyr Asn Ile Leu Thr Pro Tyr Pro Gly
        275   280   285

Pro Arg Leu His His Ser Gln Ser Pro Ala Arg Ser Leu Asn Ser Thr
    290   295   300

Pro Pro Pro Pro Pro Ala Pro Ala Pro Ala Pro Pro Pro Ala Leu Ala
305   310   315   320

Arg Pro Arg Trp Asp Arg Pro Arg Trp Asp Ser Cys Asp Ser Leu Asn
                325   330   335

Gly Leu Asp Pro Ser Glu Lys Glu Lys Phe Ser Gln Met Leu Ile Val
            340   345   350

Asn Glu Glu Leu Gln Ala Arg Leu Ala Gln Gly Arg Ser Gly Pro Ser
        355   360   365

Arg Ala Val Pro Gly Pro Arg Ala Pro Glu Pro Gln Leu Ser Pro Gly
    370   375   380

Ser Asp Ala Ser Glu Val Arg Ala Trp Leu Gln Ala Lys Gly Phe Ser
385   390   395   400

Ser Gly Thr Val Asp Ala Leu Gly Val Leu Thr Gly Ala Gln Leu Phe
                405   410   415

Ser Leu Gln Lys Glu Glu Leu Arg Ala Val Ser Pro Glu Glu Gly Ala
            420   425   430

Arg Val Tyr Ser Gln Val Thr Val Gln Arg Ser Leu Leu Glu Asp Lys
        435   440   445

Glu Lys Val Ser Glu Leu Glu Ala Val Met Glu Lys Gln Lys Lys Lys
    450   455   460

Val Glu Gly Glu Val Glu Met Glu Val Ile
465   470

<210> 262
<211> 474
<212> PRT
<213> Homo sapien

<400> 262

Asp Leu Phe Gln Met Ser Pro Leu Ser Pro Gly Ser Pro Leu Pro Pro

1 5 10 15

Leu Ala Arg Ala Asp Leu Thr Ala Ile Leu Thr Gly Cys Pro Pro Leu
20 25 30

Ser Ala Cys Leu Val Leu Ala Pro Arg Pro His Arg Arg Ala Arg Leu
35 40 45

Leu Pro Ser Glu Gly Leu Leu Thr Leu Arg Ala Lys Pro Pro Ser Glu
50 55 60

Ala Glu Tyr Thr Asp Val Leu Gln Lys Ile Lys Tyr Ala Phe Ser Leu
65 70 75 80

Leu Ala Arg Leu Arg Gly Asn Ile Ala Asp Pro Ser Ser Pro Glu Leu
85 90 95

Leu His Phe Leu Phe Gly Pro Leu Gln Met Ile Val Asn Thr Ser Gly
100 105 110

Gly Pro Glu Phe Ala Ser Ser Val Arg Arg Pro His Leu Thr Ser Asp
115 120 125

Ala Val Ala Leu Leu Arg Asp Asn Val Thr Pro Arg Glu Asn Glu Leu
130 135 140

Trp Thr Ser Leu Gly Asp Ser Trp Thr Arg Pro Gly Leu Glu Leu Ser
145 150 155 160

Pro Glu Glu Gly Pro Pro Tyr Arg Pro Glu Phe Phe Ser Gly Trp Glu
165 170 175

Pro Pro Val Thr Asp Pro Gln Ser Arg Ala Trp Glu Asp Pro Val Glu
180 185 190

Lys Gln Leu Gln His Glu Arg Arg Arg Arg Gln Gln Ser Ala Pro Gln
195 200 205

Val Ala Val Asn Gly His Arg Asp Leu Glu Pro Glu Ser Glu Pro Gln
210 215 220

Leu Glu Ser Glu Thr Ala Gly Lys Trp Val Leu Cys Asn Tyr Asp Phe
225 230 235 240

Gln Ala Arg Asn Ser Ser Glu Leu Ser Val Lys Gln Arg Asp Val Leu
245 250 255

Glu Val Leu Asp Asp Ser Arg Lys Trp Trp Lys Val Arg Asp Pro Ala
260 265 270

Gly Gln Glu Gly Tyr Val Pro Tyr Asn Ile Leu Thr Pro Tyr Pro Gly
275 280 285

Pro Arg Leu His His Ser Gln Ser Pro Ala Arg Ser Leu Asn Ser Thr
290 295 300

Pro Pro Pro Pro Pro Ala Pro Ala Pro Ala Pro Pro Pro Ala Leu Ala
305 310 315 320

Arg Pro Arg Trp Asp Arg Pro Arg Trp Asp Ser Cys Asp Ser Leu Asn
325 330 335

Gly Leu Asp Pro Ser Glu Lys Glu Lys Phe Ser Gln Met Leu Ile Val
340 345 350

Asn Glu Glu Leu Gln Ala Arg Leu Ala Gln Gly Arg Ser Gly Pro Ser
355 360 365

Arg Ala Val Pro Gly Pro Arg Ala Pro Glu Pro Gln Leu Ser Pro Gly
370 375 380

Ser Asp Ala Ser Glu Val Arg Ala Trp Leu Gln Ala Lys Gly Phe Ser
385 390 395 400

Ser Gly Thr Val Asp Ala Leu Gly Val Leu Thr Gly Ala Gln Leu Phe
405 410 415

Ser Leu Gln Lys Glu Glu Leu Arg Ala Val Ser Pro Glu Glu Gly Ala
420 425 430

Arg Val Tyr Ser Gln Val Thr Val Gln Arg Ser Leu Leu Glu Asp Lys
435 440 445

Glu Lys Val Ser Glu Leu Glu Ala Val Met Glu Lys Gln Lys Lys Lys
450 455 460

Val Glu Gly Glu Val Glu Met Glu Val Ile
465 470

<210> 263
<211> 474
<212> PRT

<213> Homo sapien

<400> 263

Asp Leu Phe Gln Met Ser Pro Leu Ser Pro Gly Ser Pro Leu Pro Pro
1 5 10 15

Leu Ala Arg Ala Asp Leu Thr Ala Ile Leu Thr Gly Cys Pro Pro Leu
20 25 30

Ser Ala Cys Leu Val Leu Ala Pro Arg Pro His Arg Arg Ala Arg Leu
35 40 45

Leu Pro Ser Glu Gly Leu Leu Thr Leu Arg Ala Lys Pro Pro Ser Glu
50 55 60

Ala Glu Tyr Thr Asp Val Leu Gln Lys Ile Lys Tyr Ala Phe Ser Leu
65 70 75 80

Leu Ala Arg Leu Arg Gly Asn Ile Ala Asp Pro Ser Ser Pro Glu Leu
85 90 95

Leu His Phe Leu Phe Gly Pro Leu Gln Met Ile Val Asn Thr Ser Gly
100 105 110

Gly Pro Glu Phe Ala Ser Ser Val Arg Arg Pro His Leu Thr Ser Asp
115 120 125

Ala Val Ala Leu Leu Arg Asp Asn Val Thr Pro Arg Glu Asn Glu Leu
130 135 140

Trp Thr Ser Leu Gly Asp Ser Trp Thr Arg Pro Gly Leu Glu Leu Ser
145 150 155 160

Pro Glu Glu Gly Pro Pro Tyr Arg Pro Glu Phe Phe Ser Gly Trp Glu
165 170 175

Pro Pro Val Thr Asp Pro Gln Ser Arg Ala Trp Glu Asp Pro Val Glu
180 185 190

Lys Gln Leu Gln His Glu Arg Arg Arg Arg Gln Gln Ser Ala Pro Gln
195 200 205

Val Ala Val Asn Gly His Arg Asp Leu Glu Pro Glu Ser Glu Pro Gln
210 215 220

Leu Glu Ser Glu Thr Ala Gly Lys Trp Val Leu Cys Asn Tyr Asp Phe

225 230 235 240

Gln Ala Arg Asn Ser Ser Glu Leu Ser Val Lys Gln Arg Asp Val Leu
245 250 255

Glu Val Leu Asp Asp Ser Arg Lys Trp Trp Lys Val Arg Asp Pro Ala
260 265 270

Gly Gln Glu Gly Tyr Val Pro Tyr Asn Ile Leu Thr Pro Tyr Pro Gly
275 280 285

Pro Arg Leu His His Ser Gln Ser Pro Ala Arg Ser Leu Asn Ser Thr
290 295 300

Pro Pro Pro Pro Pro Ala Pro Ala Pro Ala Pro Pro Pro Ala Leu Ala
305 310 315 320

Arg Pro Arg Trp Asp Arg Pro Arg Trp Asp Ser Cys Asp Ser Leu Asn
325 330 335

Gly Leu Asp Pro Ser Glu Lys Glu Lys Phe Ser Gln Met Leu Ile Val
340 345 350

Asn Glu Glu Leu Gln Ala Arg Leu Ala Gln Gly Arg Ser Gly Pro Ser
355 360 365

Arg Ala Val Pro Gly Pro Arg Ala Pro Glu Pro Gln Leu Ser Pro Gly
370 375 380

Ser Asp Ala Ser Glu Val Arg Ala Trp Leu Gln Ala Lys Gly Phe Ser
385 390 395 400

Ser Gly Thr Val Asp Ala Leu Gly Val Leu Thr Gly Ala Gln Leu Phe
405 410 415

Ser Leu Gln Lys Glu Glu Leu Arg Ala Val Ser Pro Glu Glu Gly Ala
420 425 430

Arg Val Tyr Ser Gln Val Thr Val Gln Arg Ser Leu Leu Glu Asp Lys
435 440 445

Glu Lys Val Ser Glu Leu Glu Ala Val Met Glu Lys Gln Lys Lys Lys
450 455 460

Val Glu Gly Glu Val Glu Met Glu Val Ile
465 470

<210> 264
<211> 470
<212> PRT
<213> Homo sapien

<400> 264

Met Ser Pro Leu Ser Pro Gly Ser Pro Leu Pro Pro Leu Ala Arg Ala
1 5 10 15

Asp Leu Thr Ala Ile Leu Thr Gly Cys Pro Pro Leu Ser Ala Cys Leu
20 25 30

Val Leu Ala Pro Arg Pro His Arg Arg Ala Arg Leu Leu Pro Ser Glu
35 40 45

Gly Leu Leu Thr Leu Arg Ala Lys Pro Pro Ser Glu Ala Glu Tyr Thr
50 55 60

Asp Val Leu Gln Lys Ile Lys Tyr Ala Phe Ser Leu Leu Ala Arg Leu
65 70 75 80

Arg Gly Asn Ile Ala Asp Pro Ser Ser Pro Glu Leu Leu His Phe Leu
85 90 95

Phe Gly Pro Leu Gln Met Ile Val Asn Thr Ser Gly Gly Pro Glu Phe
100 105 110

Ala Ser Ser Val Arg Arg Pro His Leu Thr Ser Asp Ala Val Ala Leu
115 120 125

Leu Arg Asp Asn Val Thr Pro Arg Glu Asn Glu Leu Trp Thr Ser Leu
130 135 140

Gly Asp Ser Trp Thr Arg Pro Gly Leu Glu Leu Ser Pro Glu Glu Gly
145 150 155 160

Pro Pro Tyr Arg Pro Glu Phe Phe Ser Gly Trp Glu Pro Pro Val Thr
165 170 175

Asp Pro Gln Ser Arg Ala Trp Glu Asp Pro Val Glu Lys Gln Leu Gln
180 185 190

His Glu Arg Arg Arg Arg Gln Gln Ser Ala Pro Gln Val Ala Val Asn
195 200 205

Gly His Arg Asp Leu Glu Pro Glu Ser Glu Pro Gln Leu Glu Ser Glu
210 215 220

Thr Ala Gly Lys Trp Val Leu Cys Asn Tyr Asp Phe Gln Ala Arg Asn
225 230 235 240

Ser Ser Glu Leu Ser Val Lys Gln Arg Asp Val Leu Glu Val Leu Asp
245 250 255

Asp Ser Arg Lys Trp Trp Lys Val Arg Asp Pro Ala Gly Gln Glu Gly
260 265 270

Tyr Val Pro Tyr Asn Ile Leu Thr Pro Tyr Pro Gly Pro Arg Leu His
275 280 285

His Ser Gln Ser Pro Ala Arg Ser Leu Asn Ser Thr Pro Pro Pro Pro
290 295 300

Pro Ala Pro Ala Pro Ala Pro Pro Pro Ala Leu Ala Arg Pro Arg Trp
305 310 315 320

Asp Arg Pro Arg Trp Asp Ser Cys Asp Ser Leu Asn Gly Leu Asp Pro
325 330 335

Ser Glu Lys Glu Lys Phe Ser Gln Met Leu Ile Val Asn Glu Glu Leu
340 345 350

Gln Ala Arg Leu Ala Gln Gly Arg Ser Gly Pro Ser Arg Ala Val Pro
355 360 365

Gly Pro Arg Ala Pro Glu Pro Gln Leu Ser Pro Gly Ser Asp Ala Ser
370 375 380

Glu Val Arg Ala Trp Leu Gln Ala Lys Gly Phe Ser Ser Gly Thr Val
385 390 395 400

Asp Ala Leu Gly Val Leu Thr Gly Ala Gln Leu Phe Ser Leu Gln Lys
405 410 415

Glu Glu Leu Arg Ala Val Ser Pro Glu Glu Gly Ala Arg Val Tyr Ser
420 425 430

Gln Val Thr Val Gln Arg Ser Leu Leu Glu Asp Lys Glu Lys Val Ser
435 440 445

Glu Leu Glu Ala Val Met Glu Lys Gln Lys Lys Lys Val Glu Gly Glu

450 455 460

Val Glu Met Glu Val Ile
465 470

<210> 265
<211> 502
<212> PRT
<213> Homo sapien

<400> 265

Met Ser Pro Leu Ser Pro Gly Ser Pro Leu Pro Pro Leu Ala Arg Ala
1 5 10 15

Asp Leu Thr Ala Ile Leu Thr Gly Cys Pro Pro Leu Ser Ala Cys Leu
20 25 30

Val Leu Ala Pro Arg Pro His Arg Arg Ala Arg Leu Leu Pro Ser Glu
35 40 45

Gly Leu Leu Thr Leu Arg Ala Lys Pro Pro Ser Glu Ala Glu Tyr Thr
50 55 60

Asp Val Leu Gln Lys Ile Lys Tyr Ala Phe Ser Leu Leu Ala Arg Leu
65 70 75 80

Arg Gly Asn Ile Ala Asp Pro Ser Ser Pro Glu Leu Leu His Phe Leu
85 90 95

Phe Gly Pro Leu Gln Met Ile Val Asn Thr Ser Gly Gly Pro Glu Phe
100 105 110

Ala Ser Ser Val Arg Arg Pro His Leu Thr Ser Asp Ala Val Ala Leu
115 120 125

Leu Arg Asp Asn Val Thr Pro Arg Glu Asn Glu Leu Trp Thr Ser Leu
130 135 140

Gly Asp Ser Trp Thr Arg Pro Gly Leu Glu Leu Ser Pro Glu Glu Gly
145 150 155 160

Pro Pro Tyr Arg Pro Glu Phe Phe Ser Gly Trp Glu Pro Pro Val Thr
165 170 175

Asp Pro Gln Ser Arg Ala Trp Glu Asp Pro Val Glu Lys Gln Leu Gln
180 185 190

His Glu Arg Arg Arg Arg Gln Val Thr Gln Ala Thr Gln Gln Gly Arg
195 200 205

Gly Trp Glu Val Arg Gly Arg Gly Arg Ser Ala Trp Pro Arg Leu Thr
210 215 220

Arg Leu Ser Tyr Phe Leu Gln Gln Ser Ala Pro Gln Val Ala Val Asn
225 230 235 240

Gly His Arg Asp Leu Glu Pro Glu Ser Glu Pro Gln Leu Glu Ser Glu
245 250 255

Thr Ala Gly Lys Trp Val Leu Cys Asn Tyr Asp Phe Gln Ala Arg Asn
260 265 270

Ser Ser Glu Leu Ser Val Lys Gln Arg Asp Val Leu Glu Val Leu Asp
275 280 285

Asp Ser Arg Lys Trp Trp Lys Val Arg Asp Pro Ala Gly Gln Glu Gly
290 295 300

Tyr Val Pro Tyr Asn Ile Leu Thr Pro Tyr Pro Gly Pro Arg Leu His
305 310 315 320

His Ser Gln Ser Pro Ala Arg Ser Leu Asn Ser Thr Pro Pro Pro Pro
325 330 335

Pro Ala Pro Ala Pro Ala Pro Pro Pro Ala Leu Ala Arg Pro Arg Trp
340 345 350

Asp Arg Pro Arg Trp Asp Ser Cys Asp Ser Leu Asn Gly Leu Asp Pro
355 360 365

Ser Glu Lys Glu Lys Phe Ser Gln Met Leu Ile Val Asn Glu Glu Leu
370 375 380

Gln Ala Arg Leu Ala Gln Gly Arg Ser Gly Pro Ser Arg Ala Val Pro
385 390 395 400

Gly Pro Arg Ala Pro Glu Pro Gln Leu Ser Pro Gly Ser Asp Ala Ser
405 410 415

Glu Val Arg Ala Trp Leu Gln Ala Lys Gly Phe Ser Ser Gly Thr Val
420 425 430

Asp Ala Leu Gly Val Leu Thr Gly Ala Gln Leu Phe Ser Leu Gln Lys
435 440 445

Glu Glu Leu Arg Ala Val Ser Pro Glu Glu Gly Ala Arg Val Tyr Ser
450 455 460

Gln Val Thr Val Gln Arg Ser Leu Leu Glu Asp Lys Glu Lys Val Ser
465 470 475 480

Glu Leu Glu Ala Val Met Glu Lys Gln Lys Lys Lys Val Glu Gly Glu
485 490 495

Val Glu Met Glu Val Ile
500

<210> 266
<211> 548
<212> PRT
<213> Homo sapien

<400> 266

Met Gly Arg Lys Ala Ile Val Leu Ala Ile Ala Asn Thr Ser Leu Ala
1 5 10 15

Phe Pro Leu Cys Gln His Leu Val Thr Phe Cys Leu Gly Glu Asp Asp
20 25 30

Gly Val His Thr Val Glu Asp Ala Ser Arg Lys Leu Ala Val Met Asp
35 40 45

Ser Gln Gly Arg Val Trp Ala Gln Glu Met Leu Leu Arg Val Ser Pro
50 55 60

Asp His Val Thr Leu Leu Asp Pro Ala Ser Lys Glu Glu Leu Glu Ser
65 70 75 80

Tyr Pro Leu Gly Ala Ile Val Arg Cys Asp Ala Val Met Pro Pro Gly
85 90 95

Arg Ser Arg Ser Leu Leu Leu Leu Val Cys Gln Glu Pro Glu Arg Ala
100 105 110

Gln Pro Asp Val His Phe Phe Gln Gly Leu Arg Leu Gly Ala Glu Leu
115 120 125

Ile Arg Glu Asp Ile Gln Gly Ala Leu His Asn Tyr Arg Ser Gly Arg
130 135 140

Gly Glu Arg Arg Ala Ala Ala Leu Arg Ala Thr Gln Glu Glu Leu Gln
145 150 155 160

Arg Asp Arg Ser Pro Ala Ala Glu Thr Pro Pro Leu Gln Arg Arg Pro
165 170 175

Ser Val Arg Ala Val Ile Ser Thr Val Glu Arg Gly Ala Gly Arg Gly
180 185 190

Arg Pro Gln Ala Lys Pro Ile Pro Glu Ala Glu Glu Ala Gln Arg Pro
195 200 205

Glu Pro Val Gly Thr Ser Ser Asn Ala Asp Ser Ala Ser Pro Asp Leu
210 215 220

Gly Pro Arg Gly Pro Asp Leu Ala Val Leu Gln Ala Glu Arg Glu Val
225 230 235 240

Asp Ile Leu Asn His Val Phe Asp Asp Val Glu Ser Phe Val Ser Arg
245 250 255

Leu Gln Lys Ser Ala Glu Ala Ala Arg Val Leu Glu His Arg Glu Arg
260 265 270

Gly Arg Arg Ser Arg Arg Arg Ala Ala Gly Glu Gly Leu Leu Thr Leu
275 280 285

Arg Ala Lys Pro Pro Ser Glu Ala Glu Tyr Thr Asp Val Leu Gln Lys
290 295 300

Ile Lys Tyr Ala Phe Ser Leu Leu Ala Arg Leu Arg Gly Asn Ile Ala
305 310 315 320

Asp Pro Ser Ser Pro Glu Leu Leu His Phe Leu Phe Gly Pro Leu Gln
325 330 335

Met Ile Val Asn Thr Ser Gly Gly Pro Glu Phe Ala Ser Ser Val Arg
340 345 350

Arg Pro His Leu Thr Ser Asp Ala Val Ala Leu Leu Arg Asp Asn Val
355 360 365

Thr Pro Arg Glu Asn Glu Leu Trp Thr Ser Leu Gly Asp Ser Trp Thr
370 375 380

Arg Pro Gly Leu Glu Leu Ser Pro Glu Glu Gly Pro Pro Tyr Arg Pro
385 390 395 400

Glu Phe Phe Ser Gly Trp Glu Pro Pro Val Thr Asp Pro Gln Ser Arg
405 410 415

Ala Trp Glu Asp Pro Val Glu Lys Gln Leu Gln His Glu Arg Arg Arg
420 425 430

Arg Gln Val Thr Gln Ala Thr Gln Gln Gly Arg Gly Trp Glu Val Arg
435 440 445

Gly Arg Gly Arg Ser Ala Trp Pro Arg Leu Thr Arg Leu Ser Tyr Phe
450 455 460

Leu Gln Gln Ser Ala Pro Gln Val Ala Val Asn Gly His Arg Asp Leu
465 470 475 480

Glu Pro Glu Ser Glu Pro Gln Leu Glu Ser Glu Thr Ala Gly Lys Trp
485 490 495

Val Leu Cys Asn Tyr Asp Phe Gln Ala Arg Asn Ser Ser Glu Leu Ser
500 505 510

Val Lys Gln Arg Asp Val Leu Glu Asp Lys Glu Lys Val Ser Glu Leu
515 520 525

Glu Ala Val Met Glu Lys Gln Lys Lys Lys Val Glu Gly Glu Val Glu
530 535 540

Met Glu Val Ile
545

<210> 267
<211> 277.
<212> PRT
<213> Homo sapien

<400> 267

Met Gly Leu Ala Ala Ser Leu Ser Pro Thr Leu Pro Leu Leu Leu Ser
1 5 10 15

His Arg Asp Leu Glu Pro Glu Ser Glu Pro Gln Leu Glu Ser Glu Thr
20 25 30

Ala Gly Lys Trp Val Leu Cys Asn Tyr Asp Phe Gln Ala Arg Asn Ser

35 40 45

Ser Glu Leu Ser Val Lys Gln Arg Asp Val Leu Glu Val Leu Asp Asp
50 55 60

Ser Arg Lys Trp Trp Lys Val Arg Asp Pro Ala Gly Gln Glu Gly Tyr
65 70 75 80

Val Pro Tyr Asn Ile Leu Thr Pro Tyr Pro Gly Pro Arg Leu His His
85 90 95

Ser Gln Ser Pro Ala Arg Ser Leu Asn Ser Thr Pro Pro Pro Pro Pro
100 105 110

Ala Pro Ala Pro Ala Pro Pro Pro Ala Leu Ala Arg Pro Arg Trp Asp
115 120 125

Arg Pro Arg Trp Asp Ser Cys Asp Ser Leu Asn Gly Leu Asp Pro Ser
130 135 140

Glu Lys Glu Lys Phe Ser Gln Met Leu Ile Val Asn Glu Glu Leu Gln
145 150 155 160

Ala Arg Leu Ala Gln Gly Arg Ser Gly Pro Ser Arg Ala Val Pro Gly
165 170 175

Pro Arg Ala Pro Glu Pro Gln Leu Ser Pro Gly Ser Asp Ala Ser Glu
180 185 190

Val Arg Ala Trp Leu Gln Ala Lys Gly Phe Ser Ser Gly Thr Val Asp
195 200 205

Ala Leu Gly Val Leu Thr Gly Ala Gln Leu Phe Ser Leu Gln Lys Glu
210 215 220

Glu Leu Arg Ala Val Ser Pro Glu Glu Gly Ala Arg Val Tyr Ser Gln
225 230 235 240

Val Thr Val Gln Arg Ser Leu Leu Glu Asp Lys Glu Lys Val Ser Glu
245 250 255

Leu Glu Ala Val Met Glu Lys Gln Lys Lys Lys Val Glu Gly Glu Val
260 265 270

Glu Met Glu Val Ile
275

<210> 268
<211> 282
<212> PRT
<213> Homo sapien

<400> 268

Met Ala Ser Leu Gly Gln Ile Leu Phe Trp Ser Ile Ile Ser Ile Ile
1 5 10 15

Ile Ile Leu Ala Gly Ala Ile Ala Leu Ile Ile Gly Phe Gly Ile Ser
20 25 30

Gly Arg His Ser Ile Thr Val Thr Thr Val Ala Ser Ala Gly Asn Ile
35 40 45

Gly Glu Asp Gly Ile Gln Ser Cys Thr Phe Glu Pro Asp Ile Lys Leu
50 55 60

Ser Asp Ile Val Ile Gln Trp Leu Lys Glu Gly Val Leu Gly Leu Val
65 70 75 80

His Glu Phe Lys Glu Gly Lys Asp Glu Leu Ser Glu Gln Asp Glu Met
85 90 95

Phe Arg Gly Arg Thr Ala Val Phe Ala Asp Gln Val Ile Val Gly Asn
100 105 110

Ala Ser Leu Arg Leu Lys Asn Val Gln Leu Thr Asp Ala Gly Thr Tyr
115 120 125

Lys Cys Tyr Ile Ile Thr Ser Lys Gly Lys Gly Asn Ala Asn Leu Glu
130 135 140

Tyr Lys Thr Gly Ala Phe Ser Met Pro Glu Val Asn Val Asp Tyr Asn
145 150 155 160

Ala Ser Ser Glu Thr Leu Arg Cys Glu Ala Pro Arg Trp Phe Pro Gln
165 170 175

Pro Thr Val Val Trp Ala Ser Gln Val Asp Gln Gly Ala Asn Phe Ser
180 185 190

Glu Val Ser Asn Thr Ser Phe Glu Leu Asn Ser Glu Asn Val Thr Met
195 200 205

Lys Val Val Ser Val Leu Tyr Asn Val Thr Ile Asn Asn Thr Tyr Ser
210 215 220

Cys Met Ile Glu Asn Asp Ile Ala Lys Ala Thr Gly Asp Ile Lys Val
225 230 235 240

Thr Glu Ser Glu Ile Lys Arg Arg Ser His Leu Gln Leu Leu Asn Ser
245 250 255

Lys Ala Ser Leu Cys Val Ser Ser Phe Phe Ala Ile Ser Trp Ala Leu
260 265 270

Leu Pro Leu Ser Pro Tyr Leu Met Leu Lys
275 280

<210> 269
<211> 59
<212> PRT
<213> Homo sapien

<400> 269

Met Ala Ser Leu Gly Gln Ile Leu Phe Trp Ser Ile Ile Ser Ile Ile
1 5 10 15

Ile Ile Leu Ala Gly Ala Ile Ala Leu Ile Ile Gly Phe Gly Ile Ser
20 25 30

Glu Val Ser Val Trp Leu Ser Ala Met Lys Gly Leu Val Val Glu Val
35 40 45

Pro Arg Leu Pro Leu Ala Leu Ile Phe Ala Ser
50 55

<210> 270
<211> 252
<212> PRT
<213> Homo sapien

<400> 270

Thr Ala Gly Arg His Ser Ile Thr Val Thr Thr Val Ala Ser Ala Gly
1 5 10 15

Asn Ile Gly Glu Asp Gly Ile Leu Ser Cys Thr Phe Glu Pro Asp Ile
20 25 30

Lys Leu Ser Asp Ile Val Ile Gln Trp Leu Lys Glu Gly Val Leu Gly
35 40 45

Leu Val His Glu Phe Lys Glu Gly Lys Asp Glu Leu Ser Glu Gln Asp
50 55 60

Glu Met Phe Arg Gly Arg Thr Ala Val Phe Ala Asp Gln Val Ile Val
65 70 75 80

Gly Asn Ala Ser Leu Arg Leu Lys Asn Val Gln Leu Thr Asp Ala Gly
85 90 95

Thr Tyr Lys Cys Tyr Ile Ile Thr Ser Lys Gly Lys Gly Asn Ala Asn
100 105 110

Leu Glu Tyr Lys Thr Gly Ala Phe Ser Met Pro Glu Val Asn Val Asp
115 120 125

Tyr Asn Ala Ser Ser Glu Thr Leu Arg Cys Glu Ala Pro Arg Trp Phe
130 135 140

Pro Gln Pro Thr Val Val Trp Ala Ser Gln Val Asp Gln Gly Ala Asn
145 150 155 160

Phe Ser Glu Val Ser Asn Thr Ser Phe Glu Leu Asn Ser Glu Asn Val
165 170 175

Thr Met Lys Val Val Ser Val Leu Tyr Asn Val Thr Ile Asn Asn Thr
180 185 190

Tyr Ser Cys Met Ile Glu Asn Asp Ile Ala Lys Ala Thr Gly Asp Ile
195 200 205

Lys Val Thr Glu Ser Glu Ile Lys Arg Arg Ser His Leu Gln Leu Leu
210 215 220

Asn Ser Lys Ala Ser Leu Cys Val Ser Ser Phe Phe Ala Ile Ser Trp
225 230 235 240

Ala Leu Leu Pro Leu Ser Pro Tyr Leu Met Leu Lys
245 250

<210> 271
<211> 155
<212> PRT
<213> Homo sapien

<400> 271

Gly Arg Gly Pro Pro Gly Glu Leu Cys His Glu Cys Trp Gln Gly Pro

1 5 10 15

Arg Leu Leu Gln Glu Gly Arg Cys Gly His Cys Ala Asp Arg Met Ala
20 25 30

Pro Trp Leu Arg Leu His Gln His His Ala Cys Cys Ser Cys Ala Val
35 40 45

Met Asp Pro Arg Ala Pro Pro Pro Ala Pro Val Pro Pro Pro Ser Pro
50 55 60

Ser Pro Ser Ile Arg Pro Ala Thr Leu Val Glu Leu Thr Leu Gly Cys
65 70 75 80

Asn Val Ala Leu Val Gly Trp Asp Thr Arg Glu Glu Asp Gln Arg Leu
85 90 95

Thr Glu Thr Trp Leu Cys Leu Gln Pro Ala Leu Val Gly Gln Pro Arg
100 105 110

Ala Trp Leu Pro Ile Met Trp Pro His Pro Ile Lys Gly Arg Arg Arg
115 120 125

Asn Ala Gly Leu Glu Ala Pro Gly Ala Arg Trp Gln Glu Gly Asp Ser
130 135 140

Phe Leu Ser Cys Val Tyr Ser Val Gln Phe Leu
145 150 155

<210> 272
<211> 107
<212> PRT
<213> Homo sapien

<400> 272

Met Val Ser Ser Val Cys Pro Pro Ser His Leu Arg Ser Ala His Gln
1 5 10 15

Val Ala Arg Tyr Arg Pro Arg Ala Pro Ile Ile Ala Val Thr Arg Asn
20 25 30

Pro Gln Thr Ala Arg Gln Ala His Leu Tyr Arg Gly Ile Phe Pro Val
35 40 45

Leu Cys Lys Asp Pro Val Gln Glu Ala Trp Ala Glu Asp Val Asp Leu
50 55 60

Arg Val Asn Phe Ala Met Asn Val Gly Lys Ala Arg Gly Phe Phe Lys
65 70 75 80

Lys Gly Asp Val Val Ile Val Leu Thr Gly Trp Arg Pro Gly Ser Gly
85 90 95

Phe Thr Asn Thr Met Arg Val Val Pro Val Pro
100 105

<210> 273
<211> 155
<212> PRT
<213> Homo sapien

<400> 273

Gly Arg Gly Pro Pro Gly Glu Leu Cys His Glu Cys Trp Gln Gly Pro
1 5 10 15

Arg Leu Leu Gln Glu Gly Arg Cys Gly His Cys Ala Asp Arg Met Ala
20 25 30

Pro Trp Leu Arg Leu His Gln His His Ala Cys Cys Ser Cys Ala Val
35 40 45

Met Asp Pro Arg Ala Pro Pro Pro Ala Pro Val Pro Pro Pro Ser Pro
50 55 60

Ser Pro Ser Ile Arg Pro Ala Thr Leu Val Glu Leu Thr Leu Gly Cys
65 70 75 80

Asn Val Ala Leu Val Gly Trp Asp Thr Arg Glu Glu Asp Gln Arg Leu
85 90 95

Thr Glu Thr Trp Leu Cys Leu Gln Pro Ala Leu Val Gly Gln Pro Arg
100 105 110

Ala Trp Leu Pro Ile Met Trp Pro His Pro Ile Lys Gly Arg Arg Arg
115 120 125

Asn Ala Gly Leu Glu Ala Pro Gly Ala Arg Trp Gln Glu Gly Asp Ser
130 135 140

Phe Leu Ser Cys Val Tyr Ser Val Gln Phe Leu
145 150 155

<210> 274

<211> 143
<212> PRT
<213> Homo sapien

<400> 274

Met Phe His Arg Lys Leu Phe Glu Glu Leu Val Arg Ala Ser Ser His
1 5 10 15

Ser Thr Asp Leu Met Glu Ala Met Ala Met Gly Ser Val Glu Ala Ser
20 25 30

Tyr Lys Cys Leu Ala Ala Ala Leu Ile Val Leu Thr Glu Ser Gly Arg
35 40 45

Ser Ala His Gln Val Ala Arg Tyr Arg Pro Arg Ala Pro Ile Ile Ala
50 55 60

Val Thr Arg Asn Pro Gln Thr Ala Arg Gln Ala His Leu Tyr Arg Gly
65 70 75 80

Ile Phe Pro Val Leu Cys Lys Asp Pro Val Gln Glu Ala Trp Ala Glu
85 90 95

Asp Val Asp Leu Arg Val Asn Phe Ala Met Asn Val Gly Lys Ala Arg
100 105 110

Gly Phe Phe Lys Lys Gly Asp Val Val Ile Val Leu Thr Gly Trp Arg
115 120 125

Pro Gly Ser Gly Phe Thr Asn Thr Met Arg Val Val Pro Val Pro
130 135 140

<210> 275
<211> 253
<212> PRT
<213> Homo sapien

<220>
<221> MISC_FEATURE
<222> (243)..(243)
<223> X=any amino acid

<220>
<221> MISC_FEATURE
<222> (245)..(245)
<223> X=any amino acid

<400> 275

Met Asp Thr Pro Pro Leu Ser Asp Ser Glu Ser Glu Ser Asp Glu Ser
1 5 10 15

Leu Val Thr Asp Arg Glu Leu Gln Asp Ala Phe Ser Arg Gly Leu Leu
20 25 30

Lys Pro Gly Leu Asn Val Val Leu Glu Gly Pro Lys Lys Ala Val Asn
35 40 45

Asp Val Asn Gly Leu Lys Gln Cys Leu Ala Glu Phe Lys Arg Asp Leu
50 55 60

Glu Trp Val Glu Arg Leu Asp Val Thr Leu Gly Pro Val Pro Glu Ile
65 70 75 80

Gly Gly Ser Glu Ala Pro Ala Pro Gln Asn Lys Asp Gln Lys Ala Val
85 90 95

Asp Pro Glu Asp Asp Phe Gln Arg Glu Met Ser Phe Tyr Arg Gln Ala
100 105 110

Gln Ala Ala Val Leu Ala Val Leu Pro Arg Leu His Gln Leu Lys Val
115 120 125

Pro Thr Lys Arg Pro Thr Asp Tyr Phe Ala Glu Met Ala Lys Ser Asp
130 135 140

Leu Gln Met Gln Lys Ile Arg Gln Lys Leu Gln Thr Lys Gln Ala Ala
145 150 155 160

Met Glu Arg Ser Glu Lys Ala Lys Gln Leu Arg Ala Leu Arg Lys Tyr
165 170 175

Gly Lys Lys Val Gln Thr Glu Val Leu Gln Lys Arg Gln Gln Glu Lys
180 185 190

Ala His Met Met Asn Ala Ile Lys Lys Tyr Gln Lys Gly Phe Ser Asp
195 200 205

Lys Leu Asp Phe Leu Glu Gly Asp Gln Lys Pro Leu Ala Gln Arg Lys
210 215 220

Lys Ala Gly Ala Lys Gly Gln Gln Met Arg Lys Gly Pro Thr Gly Pro
225 230 235 240

Gln Arg Xaa Ile Xaa Glu Lys Gly Lys Gly Ala Gln Cys

245 250

<210> 276
<211> 361
<212> PRT
<213> Homo sapien

<400> 276

Met Tyr Pro Glu Ala Leu Pro Val Gly Ile Leu Ser Asn Pro Asp Thr
1 5 10 15

Phe Lys Arg Arg Ser Gly Ser Tyr Ser Asn Asp Lys Pro Glu Val Trp
20 25 30

Phe Ala Ala Gly Ser Gly Ser Pro Asn Gln Lys Leu Ser Ser Ser Cys
35 40 45

Val Gly Arg Ala Cys Gly Glu Met Asp Thr Pro Pro Leu Ser Asp Ser
50 55 60

Glu Ser Glu Ser Asp Glu Ser Leu Val Thr Asp Arg Glu Leu Gln Asp
65 70 75 80

Ala Phe Ser Arg Gly Leu Leu Lys Pro Gly Leu Asn Val Val Leu Glu
85 90 95

Gly Pro Lys Lys Ala Val Asn Asp Val Asn Gly Leu Lys Gln Cys Leu
100 105 110

Ala Glu Phe Lys Arg Asp Leu Glu Trp Val Glu Arg Leu Asp Val Thr
115 120 125

Leu Gly Pro Val Pro Glu Ile Gly Gly Ser Glu Ala Pro Ala Pro Gln
130 135 140

Asn Lys Asp Gln Lys Ala Val Asp Pro Glu Asp Asp Phe Gln Arg Glu
145 150 155 160

Met Ser Phe Tyr Arg Gln Ala Gln Ala Ala Val Leu Ala Val Leu Pro
165 170 175

Arg Leu His Gln Leu Lys Val Pro Thr Lys Arg Pro Thr Asp Tyr Phe
180 185 190

Ala Glu Met Ala Lys Ser Asp Leu Gln Met Gln Lys Ile Arg Gln Lys
195 200 205

Leu Gln Thr Lys Gln Ala Ala Met Glu Arg Ser Glu Lys Ala Lys Gln
210 215 220

Leu Arg Ala Leu Arg Lys Tyr Gly Lys Lys Val Gln Thr Glu Val Leu
225 230 235 240

Gln Lys Arg Gln Gln Glu Lys Ala His Met Met Asn Ala Ile Lys Lys
245 250 255

Tyr Gln Lys Gly Phe Ser Asp Lys Leu Asp Phe Leu Glu Gly Asp Gln
260 265 270

Lys Pro Leu Ala Gln Arg Lys Lys Ala Gly Ala Lys Gly Gln Gln Met
275 280 285

Arg Lys Gly Pro Ser Ala Lys Arg Arg Tyr Lys Asn Gln Lys Phe Gly
290 295 300

Phe Gly Gly Lys Lys Lys Gly Ser Lys Trp Asn Thr Arg Glu Ser Tyr
305 310 315 320

Asp Asp Val Ser Ser Phe Arg Ala Lys Thr Ala His Gly Arg Gly Leu
325 330 335

Lys Arg Pro Gly Lys Lys Gly Ser Asn Lys Arg Pro Gly Lys Arg Thr
340 345 350

Arg Glu Lys Met Lys Asn Arg Thr His
355 360

<210> 277
<211> 167
<212> PRT
<213> Homo sapien

<400> 277

Met Ala Lys Ser Asp Leu Gln Met Gln Lys Ile Arg Gln Lys Leu Gln
1 5 10 15

Thr Lys Gln Ala Ala Met Glu Arg Ser Glu Lys Ala Lys Gln Leu Arg
20 25 30

Ala Leu Arg Lys Tyr Gly Lys Lys Val Gln Thr Glu Val Leu Gln Lys
35 40 45

Arg Gln Gln Glu Lys Ala His Met Met Asn Ala Ile Lys Lys Tyr Gln

50 55 60

Lys Gly Phe Ser Asp Lys Leu Asp Phe Leu Glu Gly Asp Gln Lys Pro
65 70 75 80

Leu Ala Gln Arg Lys Lys Ala Gly Ala Lys Gly Gln Gln Met Arg Lys
85 90 95

Gly Pro Ser Ala Lys Arg Arg Tyr Lys Asn Gln Lys Phe Gly Phe Gly
100 105 110

Gly Lys Lys Lys Gly Ser Lys Trp Asn Thr Arg Glu Ser Tyr Asp Asp
115 120 125

Val Ser Ser Phe Arg Ala Lys Thr Ala His Gly Arg Gly Leu Lys Arg
130 135 140

Pro Gly Lys Lys Gly Ser Asn Lys Arg Pro Gly Lys Arg Thr Arg Glu
145 150 155 160

Lys Met Lys Asn Arg Thr His
165

<210> 278
<211> 636
<212> PRT
<213> Homo sapien

<400> 278

Pro Arg Arg Gly Leu Arg Val Ser Ser Pro Gly Gly Pro Gly Ala Met
1 5 10 15

Gly Trp Val Gly Gly Arg Arg Arg Asp Ser Ala Ser Pro Pro Gly Arg
20 25 30

Ser Arg Ser Ala Ala Asp Asp Ile Asn Pro Ala Pro Ala Asn Met Glu
35 40 45

Gly Gly Gly Gly Ser Val Ala Val Ala Gly Leu Gly Ala Arg Gly Ser
50 55 60

Gly Ala Ala Ala Ala Thr Val Arg Glu Leu Leu Gln Asp Gly Cys Tyr
65 70 75 80

Ser Asp Phe Leu Asn Glu Asp Phe Asp Val Lys Thr Tyr Thr Ser Gln
85 90 95

Ser Ile His Gln Ala Val Ile Ala Glu Gln Leu Ala Lys Leu Ala Gln
100 105 110

Gly Ile Ser Gln Leu Asp Arg Glu Leu His Leu Gln Val Val Ala Arg
115 120 125

His Glu Asp Leu Leu Ala Gln Ala Thr Gly Ile Glu Ser Leu Glu Gly
130 135 140

Val Leu Gln Met Met Gln Thr Arg Ile Gly Ala Leu Gln Gly Ala Val
145 150 155 160

Asp Arg Ile Lys Ala Lys Ile Val Glu Pro Tyr Asn Lys Ile Val Ala
165 170 175

Arg Thr Ala Gln Leu Ala Arg Leu Gln Val Ala Cys Asp Leu Leu Arg
180 185 190

Arg Ile Ile Arg Ile Leu Asn Leu Ser Lys Arg Leu Gln Gly Gln Leu
195 200 205

Gln Gly Gly Ser Arg Glu Ile Thr Lys Ala Ala Gln Ser Leu Asn Glu
210 215 220

Leu Asp Tyr Leu Ser Gln Gly Ile Asp Leu Ser Gly Ile Glu Val Ile
225 230 235 240

Glu Asn Asp Leu Leu Phe Ile Ala Arg Ala Arg Leu Glu Val Glu Asn
245 250 255

Gln Ala Lys Arg Leu Leu Glu Gln Gly Leu Glu Thr Gln Asn Pro Thr
260 265 270

Gln Val Gly Thr Ala Leu Gln Val Phe Tyr Asn Leu Gly Thr Leu Lys
275 280 285

Asp Thr Ile Thr Ser Val Val Asp Gly Tyr Cys Ala Thr Leu Glu Glu
290 295 300

Asn Ile Asn Ser Ala Leu Asp Ile Lys Val Leu Thr Gln Pro Ser Gln
305 310 315 320

Ser Ala Val Arg Gly Gly Pro Gly Arg Ser Thr Met Pro Thr Pro Gly
325 330 335

Asn Thr Ala Ala Leu Arg Ala Ser Leu Trp Thr Asn Met Glu Lys Leu
340 345 350

Met Asp His Ile Tyr Ala Val Cys Gly Gln Val Gln His Leu Gln Lys
355 360 365

Val Leu Ala Lys Lys Arg Asp Pro Val Ser His Ile Cys Phe Ile Glu
370 375 380

Glu Ile Val Lys Asp Gly Gln Pro Glu Ile Phe Tyr Thr Phe Trp Asn
385 390 395 400

Ser Val Thr Gln Ala Leu Ser Ser Gln Phe His Met Ala Thr Asn Ser
405 410 415

Ser Met Phe Leu Lys Gln Ala Phe Glu Gly Glu Tyr Pro Lys Leu Leu
420 425 430

Arg Leu Tyr Asn Asp Leu Trp Lys Arg Leu Gln Gln Tyr Ser Gln His
435 440 445

Ile Gln Gly Asn Phe Asn Ala Ser Gly Thr Thr Asp Leu Tyr Val Asp
450 455 460

Leu Gln His Met Glu Asp Asp Ala Gln Asp Ile Phe Ile Pro Lys Lys
465 470 475 480

Pro Asp Tyr Asp Pro Glu Lys Ala Leu Lys Asp Ser Leu Gln Pro Tyr
485 490 495

Glu Ala Ala Tyr Leu Ser Lys Ser Leu Ser Arg Leu Phe Asp Pro Ile
500 505 510

Asn Leu Val Phe Pro Pro Gly Gly Arg Asn Pro Pro Ser Ser Asp Glu
515 520 525

Leu Asp Gly Ile Ile Lys Thr Ile Ala Ser Glu Leu Asn Val Ala Ala
530 535 540

Val Asp Thr Asn Leu Thr Leu Ala Val Ser Lys Asn Val Ala Lys Thr
545 550 555 560

Ile Gln Leu Tyr Ser Val Lys Ser Glu Gln Leu Leu Ser Thr Gln Gly
565 570 575

Asp Ala Ser Gln Val Ile Gly Pro Leu Thr Glu Gly Gln Arg Arg Asn

580 585 590

Val Ala Val Val Asn Ser Leu Tyr Lys Leu His Gln Ser Val Thr Lys
595 600 605

Val Val Ser Ser Gln Ser Ser Phe Pro Leu Ala Ala Glu Gln Thr Ile
610 615 620

Ile Ser Ala Leu Lys Asp Leu Gln Tyr Ser Val Glu
625 630 635

<210> 279
<211> 870
<212> PRT
<213> Homo sapien

<400> 279

Met Gly Trp Val Gly Gly Arg Arg Arg Asp Ser Ala Ser Pro Pro Gly
1 5 10 15

Arg Ser Arg Ser Ala Ala Asp Asp Ile Asn Pro Ala Pro Ala Asn Met
20 25 30

Glu Gly Gly Gly Gly Ser Val Ala Val Ala Gly Leu Gly Ala Arg Gly
35 40 45

Ser Gly Ala Ala Ala Ala Thr Val Arg Glu Leu Leu Gln Asp Gly Cys
50 55 60

Tyr Ser Asp Phe Leu Asn Glu Asp Phe Asp Val Lys Thr Tyr Thr Ser
65 70 75 80

Gln Ser Ile His Gln Ala Val Ile Ala Glu Gln Leu Ala Lys Leu Ala
85 90 95

Gln Gly Ile Ser Gln Leu Asp Arg Glu Leu His Leu Gln Val Val Ala
100 105 110

Arg His Glu Asp Leu Leu Ala Gln Ala Thr Gly Ile Glu Ser Leu Glu
115 120 125

Gly Val Leu Gln Met Met Gln Thr Arg Ile Gly Ala Leu Gln Gly Ala
130 135 140

Val Asp Arg Ile Lys Ala Lys Ile Val Glu Pro Tyr Asn Lys Ile Val
145 150 155 160

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Ala Arg Thr Ala Gln Leu Ala Arg Leu Gln Val Ala Cys Asp Leu Leu
                165                 170                 175

Arg Arg Ile Ile Arg Ile Leu Asn Leu Ser Lys Arg Leu Gln Gly Gln
            180                 185                 190

Leu Gln Gly Gly Ser Arg Glu Ile Thr Lys Ala Ala Gln Ser Leu Asn
        195                 200                 205

Glu Leu Asp Tyr Leu Ser Gln Gly Ile Asp Leu Ser Gly Ile Glu Val
    210                 215                 220

Ile Glu Asn Asp Leu Leu Phe Ile Ala Arg Ala Arg Leu Glu Val Glu
225                 230                 235                 240

Asn Gln Ala Lys Arg Leu Leu Glu Gln Gly Leu Glu Thr Gln Asn Pro
                245                 250                 255

Thr Gln Val Gly Thr Ala Leu Gln Val Phe Tyr Asn Leu Gly Thr Leu
            260                 265                 270

Lys Asp Thr Ile Thr Ser Val Val Asp Gly Tyr Cys Ala Thr Leu Glu
        275                 280                 285

Glu Asn Ile Asn Ser Ala Leu Asp Ile Lys Val Leu Thr Gln Pro Ser
    290                 295                 300

Gln Ser Ala Val Arg Gly Gly Pro Gly Arg Ser Thr Met Pro Thr Pro
305                 310                 315                 320

Gly Asn Thr Ala Ala Leu Arg Ala Ser Leu Trp Thr Asn Met Glu Lys
                325                 330                 335

Leu Met Asp His Ile Tyr Ala Val Cys Gly Gln Val Gln His Leu Gln
            340                 345                 350

Lys Val Leu Ala Lys Lys Arg Asp Pro Val Ser His Ile Cys Phe Ile
        355                 360                 365

Glu Glu Ile Val Lys Asp Gly Gln Pro Glu Ile Phe Tyr Thr Phe Trp
    370                 375                 380

Asn Ser Val Thr Gln Ala Leu Ser Ser Gln Phe His Met Ala Thr Asn
385                 390                 395                 400
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Ser Ser Met Phe Leu Lys Gln Ala Phe Glu Gly Glu Tyr Pro Lys Leu
405 410 415

Leu Arg Leu Tyr Asn Asp Leu Trp Lys Arg Leu Gln Gln Tyr Ser Gln
420 425 430

His Ile Gln Gly Asn Phe Asn Ala Ser Gly Thr Thr Asp Leu Tyr Val
435 440 445

Asp Leu Gln His Met Glu Asp Asp Ala Gln Asp Ile Phe Ile Pro Lys
450 455 460

Lys Pro Asp Tyr Asp Pro Glu Lys Ala Leu Lys Asp Ser Leu Gln Pro
465 470 475 480

Tyr Glu Ala Ala Tyr Leu Ser Lys Ser Leu Ser Arg Leu Phe Asp Pro
485 490 495

Ile Asn Leu Val Phe Pro Pro Gly Gly Arg Asn Pro Pro Ser Ser Asp
500 505 510

Glu Leu Asp Gly Ile Ile Lys Thr Ile Ala Ser Glu Leu Asn Val Ala
515 520 525

Ala Val Asp Thr Asn Leu Thr Leu Ala Val Ser Lys Asn Val Ala Lys
530 535 540

Thr Ile Gln Leu Tyr Ser Val Lys Ser Glu Gln Leu Leu Ser Thr Gln
545 550 555 560

Gly Asp Ala Ser Gln Val Ile Gly Pro Leu Thr Glu Gly Gln Arg Arg
565 570 575

Asn Val Ala Val Val Asn Ser Leu Tyr Lys Leu His Gln Ser Val Thr
580 585 590

Lys Val Val Ser Ser Gln Ser Ser Phe Pro Leu Ala Ala Glu Gln Thr
595 600 605

Ile Ile Ser Ala Leu Lys Asp Leu Gln Tyr Ser Val Glu Tyr Glu Leu
610 615 620

Ala Ile His Ala Leu Met Glu Asn Ala Val Gln Pro Leu Leu Thr Ser
625 630 635 640

Val Gly Asp Ala Ile Glu Ala Ile Ile Ile Thr Met His Gln Glu Asp

645 650 655

Phe Ser Gly Ser Leu Ser Ser Ser Gly Lys Pro Asp Val Pro Cys Ser
660 665 670

Leu Tyr Met Lys Glu Leu Gln Gly Phe Ile Ala Arg Val Met Ser Asp
675 680 685

Tyr Phe Lys His Phe Glu Cys Leu Asp Phe Val Phe Asp Asn Thr Glu
690 695 700

Ala Ile Ala Gln Arg Ala Val Glu Leu Phe Ile Arg His Ala Ser Leu
705 710 715 720

Ile Arg Pro Leu Gly Glu Gly Gly Lys Met Arg Leu Ala Ala Asp Phe
725 730 735

Ala Gln Met Glu Leu Ala Val Gly Pro Phe Cys Arg Arg Val Ser Asp
740 745 750

Leu Gly Lys Ser Tyr Arg Met Leu Arg Ser Phe Arg Pro Leu Leu Phe
755 760 765

Gln Ala Ser Glu His Val Ala Ser Ser Pro Ala Leu Gly Asp Val Ile
770 775 780

Pro Phe Ser Ile Ile Ile Gln Phe Leu Phe Thr Arg Ala Pro Ala Glu
785 790 795 800

Leu Lys Ser Pro Phe Gln Arg Ala Glu Trp Ser His Thr Arg Phe Ser
805 810 815

Gln Trp Leu Asp Asp His Pro Ser Glu Lys Asp Arg Leu Leu Leu Ile
820 825 830

Arg Gly Ala Leu Glu Ala Tyr Val Gln Ser Val Arg Ser Arg Glu Gly
835 840 845

Lys Glu Phe Ala Pro Val Tyr Pro Ile Met Val Gln Leu Leu Gln Lys
850 855 860

Ala Met Ser Ala Leu Gln
865 870

<210> 280
<211> 791

<212> PRT
<213> Homo sapien

<400> 280

Met Gly Trp Val Gly Gly Arg Arg Arg Asp Ser Ala Ser Pro Pro Gly
1 5 10 15

Arg Ser Arg Ser Ala Ala Asp Asp Ile Asn Pro Ala Pro Ala Asn Met
20 25 30

Glu Gly Gly Gly Gly Ser Val Ala Val Ala Gly Leu Gly Ala Arg Gly
35 40 45

Ser Gly Ala Ala Ala Ala Thr Val Arg Glu Leu Leu Gln Asp Gly Cys
50 55 60

Tyr Ser Asp Phe Leu Asn Glu Asp Phe Asp Val Lys Thr Tyr Thr Ser
65 70 75 80

Gln Ser Ile His Gln Ala Val Ile Ala Glu Gln Leu Ala Lys Leu Ala
85 90 95

Gln Gly Ile Ser Gln Leu Asp Arg Glu Leu His Leu Gln Val Val Ala
100 105 110

Arg His Glu Asp Leu Leu Ala Gln Ala Thr Gly Ile Glu Ser Leu Glu
115 120 125

Gly Val Leu Gln Met Met Gln Thr Arg Ile Gly Ala Leu Gln Gly Ala
130 135 140

Val Asp Arg Ile Lys Ala Lys Ile Val Glu Pro Tyr Asn Lys Ile Val
145 150 155 160

Ala Arg Thr Ala Gln Leu Ala Arg Leu Gln Val Ala Cys Asp Leu Leu
165 170 175

Arg Arg Ile Ile Arg Ile Leu Asn Leu Ser Lys Arg Leu Gln Gly Gln
180 185 190

Leu Gln Gly Gly Ser Arg Glu Ile Thr Lys Ala Ala Gln Ser Leu Asn
195 200 205

Glu Leu Asp Tyr Leu Ser Gln Gly Ile Asp Leu Ser Gly Ile Glu Val
210 215 220

Ile Glu Asn Asp Leu Leu Phe Ile Ala Arg Ala Arg Leu Glu Val Glu
225 230 235 240

Asn Gln Ala Lys Arg Leu Leu Glu Gln Gly Leu Glu Thr Gln Asn Pro
245 250 255

Thr Gln Val Gly Thr Ala Leu Gln Val Phe Tyr Asn Leu Gly Thr Leu
260 265 270

Lys Asp Thr Ile Thr Ser Val Val Asp Gly Tyr Cys Ala Thr Leu Glu
275 280 285

Glu Asn Ile Asn Ser Ala Leu Asp Ile Lys Val Leu Thr Gln Pro Ser
290 295 300

Gln Ser Ala Val Arg Gly Gly Pro Gly Arg Ser Thr Met Pro Thr Pro
305 310 315 320

Gly Asn Thr Ala Ala Leu Arg Ala Ser Leu Trp Thr Asn Met Glu Lys
325 330 335

Leu Met Asp His Ile Tyr Ala Val Cys Gly Gln Val Gln His Leu Gln
340 345 350

Lys Val Leu Ala Lys Lys Arg Asp Pro Val Ser His Ile Cys Phe Ile
355 360 365

Glu Glu Ile Val Lys Asp Gly Gln Pro Glu Ile Phe Tyr Thr Phe Trp
370 375 380

Asn Ser Val Thr Gln Ala Leu Ser Ser Gln Phe His Met Ala Thr Asn
385 390 395 400

Ser Ser Met Phe Leu Lys Gln Ala Phe Glu Gly Glu Tyr Pro Lys Leu
405 410 415

Leu Arg Leu Tyr Asn Asp Leu Trp Lys Arg Leu Gln Gln Tyr Ser Gln
420 425 430

His Ile Gln Gly Asn Phe Asn Ala Ser Gly Thr Thr Asp Leu Tyr Val
435 440 445

Asp Leu Gln His Met Glu Asp Asp Ala Gln Asp Ile Phe Ile Pro Lys
450 455 460

Lys Pro Asp Tyr Asp Pro Glu Lys Ala Leu Lys Asp Ser Leu Gln Pro

465 470 475 480

Tyr Glu Ala Ala Tyr Leu Ser Lys Ser Leu Ser Arg Leu Phe Asp Pro
485 490 495

Ile Asn Leu Val Phe Pro Pro Gly Gly Arg Asn Pro Pro Ser Ser Asp
500 505 510

Glu Leu Asp Gly Ile Ile Lys Thr Ile Ala Ser Glu Leu Asn Val Ala
515 520 525

Ala Val Asp Thr Asn Leu Thr Leu Ala Val Ser Lys Asn Val Ala Lys
530 535 540

Thr Ile Gln Leu Tyr Ser Val Lys Ser Glu Gln Leu Leu Ser Thr Gln
545 550 555 560

Gly Asp Ala Ser Gln Val Ile Gly Pro Leu Thr Glu Gly Gln Arg Arg
565 570 575

Asn Val Ala Val Val Asn Ser Leu Tyr Lys Leu His Gln Ser Val Thr
580 585 590

Lys Val Val Ser Ser Gln Ser Ser Phe Pro Leu Ala Ala Glu Gln Thr
595 600 605

Ile Ile Ser Ala Leu Lys Ala Ile His Ala Leu Met Glu Asn Ala Val
610 615 620

Gln Pro Leu Leu Thr Ser Val Gly Asp Ala Ile Glu Ala Ile Ile Ile
625 630 635 640

Thr Met His Gln Glu Asp Phe Ser Gly Ser Leu Ser Ser Ser Gly Lys
645 650 655

Pro Asp Val Pro Cys Ser Leu Tyr Met Lys Glu Leu Gln Gly Phe Ile
660 665 670

Ala Arg Val Met Ser Asp Tyr Phe Lys His Phe Glu Cys Leu Asp Phe
675 680 685

Val Phe Asp Asn Thr Glu Ala Ile Ala Gln Arg Ala Val Glu Leu Phe
690 695 700

Ile Arg His Ala Ser Leu Ile Arg Pro Leu Gly Glu Gly Gly Lys Met
705 710 715 720

Arg Leu Ala Ala Asp Phe Ala Gln Met Glu Leu Ala Val Gly Pro Phe
725 730 735

Cys Arg Arg Val Ser Asp Leu Gly Lys Ser Tyr Arg Met Leu Arg Ser
740 745 750

Phe Arg Gly Ala Leu Glu Ala Tyr Val Gln Ser Val Arg Ser Arg Glu
755 760 765

Gly Lys Glu Phe Ala Pro Val Tyr Pro Ile Met Val Gln Leu Leu Gln
770 775 780

Lys Ala Met Ser Ala Leu Gln
785 790

<210> 281
<211> 122
<212> PRT
<213> Homo sapien

<400> 281

Lys Val Thr Gly Lys Ser Gln Thr Val Leu Ala Ser Gly Val Asp Glu
1 5 10 15

Lys Gln Ala Lys Ile Ser Ser Pro Thr Glu Thr Glu Arg Cys Ile Glu
20 25 30

Ser Leu Ile Ala Val Phe Gln Lys Tyr Ala Gly Lys Asp Gly Tyr Asn
35 40 45

Tyr Thr Leu Ser Lys Thr Glu Phe Leu Ser Phe Met Asn Thr Glu Leu
50 55 60

Ala Ala Phe Thr Lys Asn Gln Lys Asp Pro Gly Val Leu Asp Arg Met
65 70 75 80

Met Lys Lys Leu Asp Thr Asn Ser Asp Gly Gln Leu Asp Phe Ser Glu
85 90 95

Phe Leu Asn Leu Ile Gly Gly Leu Ala Met Ala Cys His Asp Ser Phe
100 105 110

Leu Lys Ala Val Pro Ser Gln Lys Arg Thr
115 120

<210> 282
<211> 170
<212> PRT
<213> Homo sapien

<400> 282

His Arg Pro Ser Ser Thr His Cys Asp Leu Gln Pro Ala Leu Phe Val
1 5 10 15

Ser Ser Leu Pro Phe Lys Arg Gln Leu Ala Leu Glu Gly His Leu Leu
20 25 30

Ser Ser Leu Pro Leu Asp Thr Pro Thr Lys Thr Gln Gly Glu Ala Leu
35 40 45

Lys Ser Asn Trp Lys Val Thr Asp Arg Ser Gly Lys Trp Ile Asp Glu
50 55 60

Lys Gln Ala Lys Ile Ser Ser Pro Thr Glu Thr Glu Arg Cys Ile Glu
65 70 75 80

Ser Leu Ile Ala Val Phe Gln Lys Tyr Ala Gly Lys Asp Gly Tyr Asn
85 90 95

Tyr Thr Leu Ser Lys Thr Glu Phe Leu Ser Phe Met Asn Thr Glu Leu
100 105 110

Ala Ala Phe Thr Lys Asn Gln Lys Asp Pro Gly Val Leu Asp Arg Met
115 120 125

Met Lys Lys Leu Asp Thr Asn Ser Asp Gly Gln Leu Asp Phe Ser Glu
130 135 140

Phe Leu Asn Leu Ile Gly Gly Leu Ala Met Ala Cys His Asp Ser Phe
145 150 155 160

Leu Lys Ala Val Pro Ser Gln Lys Arg Thr
165 170

<210> 283
<211> 91
<212> PRT
<213> Homo sapien

<400> 283

Met Lys Leu Glu Glu Leu Cys Leu Lys Tyr Ala Gly Lys Asp Gly Tyr
1 5 10 15

Asn Tyr Thr Leu Ser Lys Thr Glu Phe Leu Ser Phe Met Asn Thr Glu
20 25 30

Leu Ala Ala Phe Thr Lys Asn Gln Lys Asp Pro Gly Val Leu Asp Arg
35 40 45

Met Met Lys Lys Leu Asp Thr Asn Ser Asp Gly Gln Leu Asp Phe Ser
50 55 60

Glu Phe Leu Asn Leu Ile Gly Gly Leu Ala Met Ala Cys His Asp Ser
65 70 75 80

Phe Leu Lys Ala Val Pro Ser Gln Lys Arg Thr
85 90

<210> 284
<211> 66
<212> PRT
<213> Homo sapien

<400> 284

Ser Leu Cys Tyr Asn Val Leu Lys Pro Pro Tyr Tyr Arg Asn Ile Tyr
1 5 10 15

Tyr Ile Phe Ser Ile Cys Ser Phe Ser Glu Gly Leu Trp Ile Ser Leu
20 25 30

Asn Cys Gln Ile Leu Ala Tyr Phe Cys Asp Thr Pro Ala His Phe Leu
35 40 45

Ser Leu Ile Asn Gln Gly Val Arg Cys Asp Cys His Asn Cys Tyr Val
50 55 60

Phe Gln
65

<210> 285
<211> 65
<212> PRT
<213> Homo sapien

<400> 285

Met Pro Gln Tyr Gln Thr Trp Glu Glu Phe Ser Arg Ala Ala Glu Lys
1 5 10 15

Leu Tyr Leu Ala Asp Pro Met Lys Ala Arg Val Val Leu Lys Tyr Arg
20 25 30

His Ser Asp Gly Asn Leu Cys Val Lys Val Thr Asp Asp Leu Val Leu
35 40 45

Met Arg Leu Met Val Ala Lys Glu Ala Arg Asn Val Thr Met Glu Thr
50 55 60

Glu
65

<210> 286
<211> 363
<212> PRT
<213> Homo sapien

<400> 286

Ser Arg Thr Thr Ser Ser Ser Ser Ser Arg Ala Thr Trp Cys Pro Leu
1 5 10 15

Thr Leu Ser Glu Gly Arg Leu Pro Gly Thr Gln Thr Leu Arg Glu Gln
20 25 30

Asn Gly Gln Pro Glu Leu Gly Lys Pro Arg Thr Asp Phe Lys Gly Ser
35 40 45

Phe Trp Thr Gly Gly Gly Arg Gly Pro Phe Pro Arg Gly Thr Asn Lys
50 55 60

Pro Ser Val Gln Asn Glu Gly Leu Cys Cys Ala Ser Arg Arg Ala Ser
65 70 75 80

Trp Arg Arg Gln Pro Leu Glu Val Ser His Leu Leu Pro Lys His Pro
85 90 95

Gln Val Val Asp Asp His Thr Ala Lys Lys Val Ser Gly Ile Leu Lys
100 105 110

Arg His Leu Gln Pro Val His Phe Ser Ser Trp Tyr Gly Glu Ser Val
115 120 125

Ser Val Gly Ser Gln Gly Lys Leu Val Ile Ser Gly Phe Pro Pro Ala
130 135 140

Gly Pro His Pro Phe Gln Thr Gln Leu Thr Leu His Arg Cys Gly Gln
145 150 155 160

Pro Gly Glu Ala Ala Gly Pro Ser Lys Pro Leu Thr Gln Asn Arg Trp
165 170 175

Ser Ser Ala Pro Phe Tyr Arg Lys Ser Gly Val Leu Glu Val Thr Cys
180 185 190

Ser Arg Ser His Ile Arg Val Pro Ile Arg Val Trp Val Ser Pro Lys
195 200 205

Leu Pro Glu Ala Gln Thr Thr His Pro Arg Ser Arg Gly Arg Ile Ser
210 215 220

Glu Ala Ser Cys Cys Pro Gln Gly Arg Asn Leu Gln Ser Cys Gly Glu
225 230 235 240

Pro Glu Cys Pro Val Asn Leu Gln Gln Arg Lys Ala Met Ser Val Trp
245 250 255

Gly Asp Pro Trp Asn Pro Cys His Pro Gly Pro Ser Ser Thr Phe Gln
260 265 270

Ala Ala Pro Ala Thr Gly Glu Ala Thr Leu Lys Leu Asp Leu Gln Leu
275 280 285

Gly Asp Thr Asp Glu Leu Gly Lys Leu Gln Arg His Pro Leu Gly Gly
290 295 300

Ala Leu Glu Ala Asp Arg Glu Thr Glu Ala Gln Ala His Cys Arg His
305 310 315 320

Arg Ala Leu Leu Cys Leu Ser His Ser His Ser Ser Trp Asn Gly Gly
325 330 335

Glu Glu Gly Asn Ser Ala His Val Pro Phe Leu Val Glu Lys Met Phe
340 345 350

Phe Ser Lys Leu Pro Ser Val Ala Ile Gln His
355 360

<210> 287
<211> 116
<212> PRT
<213> Homo sapien

<400> 287

Cys Pro Gly Ser Ser Phe His Glu Ser His Asn Ser His Phe Leu Leu
1 5 10 15

Gly Arg Lys Tyr Phe Tyr Ile Asn Ser Glu Lys Leu Gln Lys Cys Ile
20 25 30

Phe Thr Asn Leu Gly Glu Val Glu Val Pro Gly Val Ser Pro Arg Phe
35 40 45

Ser Gln Leu Cys Ser Val Met Gln Val Ser Ala Arg Val Pro Val Cys
50 55 60

Pro Leu Arg Gly Glu Arg Arg Leu Ala Cys Ala Ser Thr Pro Leu Pro
65 70 75 80

Ile Gln Ala His Ser Pro Pro Phe Pro Cys Pro Ile Ser Val Gln Gln
85 90 95

Val Ile Glu Asn His Ile Leu Lys Leu Phe Gln Ser Asn Leu Val Pro
100 105 110

Ala Asp Pro Glu
115

<210> 288
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<212> PRT
<213> Homo sapien

<400> 288

Pro His Gly Gln Lys Ser Gln Trp His Pro Gln Thr Ser Pro Ser Ala
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Gly Pro Leu Gln Gln Leu Val Trp Gly Lys Ser Glu Ala Ser Cys Cys
20 25 30

Pro Gln Gly Arg Asn Leu Gln Ser Cys Gly Glu Pro Glu Cys Pro Val
35 40 45

Asn Leu Gln Gln Arg Lys Ala Met Ser Val Trp Gly Asp Pro Trp Asn
50 55 60

Pro Cys His Pro Gly Pro Ser Ser Thr Phe Gln Ala Ala Pro Ala Thr
65 70 75 80

Gly Glu Ala Thr Leu Lys Leu Asp Leu Gln Leu Gly Asp Thr Asp Glu
85 90 95

Leu Gly Lys Leu Gln Arg His Pro Leu Gly Gly Ala Leu Glu Ala Asp
100 105 110

Arg Glu Thr Glu Ala Gln Ala His Cys Arg His Arg Ala Leu Leu Cys
115 120 125

Leu Ser His Ser His Ser Ser Trp Asn Gly Gly Glu Glu Gly Asn Ser
130 135 140

Ala His Val Pro Phe Leu Val Glu Lys Met Phe Phe Ser Lys Leu Pro
145 150 155 160

Ser Val Ala Ile Gln His
165

<210> 289
<211> 207
<212> PRT
<213> Homo sapien

<400> 289

Ala Ser Pro Leu Arg Ala Ala Leu Gly Leu Arg Ser Leu Val Cys Ala
1 5 10 15

Leu Val Arg Pro Pro Val Leu Ser Thr Arg Ala Trp Pro Pro Asp Asp
20 25 30

Ala Gly Ala Ala Arg Ala Gly Arg Gly Ser Leu Arg Ser Leu Leu Pro
35 40 45

Ser Ala Gly Pro Leu Arg Arg Ser Pro Gln Phe Pro Ala Arg Thr Arg
50 55 60

Ser Gly Pro Pro Asn Leu Arg Pro Lys Ser Gly Gly Gly Ser Gly Gly
65 70 75 80

Lys Lys Met Lys Asn Glu Ile Ala Ala Val Val Phe Phe Phe Thr Arg
85 90 95

Leu Val Arg Lys His Asp Lys Leu Lys Lys Glu Ala Val Glu Arg Phe
100 105 110

Ala Glu Lys Leu Thr Leu Ile Leu Gln Glu Lys Tyr Lys Asn His Trp
115 120 125

Tyr Pro Glu Lys Pro Ser Lys Gly Gln Ala Tyr Arg Cys Ile Arg Val
130 135 140

Asn Lys Phe Gln Arg Val Asp Pro Asp Val Leu Lys Ala Cys Glu Asn
145 150 155 160

Ser Cys Ile Leu Tyr Ser Asp Leu Gly Leu Pro Lys Glu Leu Thr Leu
165 170 175

Trp Val Asp Pro Cys Glu Val Cys Cys Arg Tyr Gly Glu Lys Asn Asn
180 185 190

Ala Phe Ile Val Ala Ser Phe Glu Asn Lys Asp Glu Gly Tyr Leu
195 200 205

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<400> 290

Met Ala Val Trp Ser Pro Leu Val Met Pro Gly Arg Arg Glu Gly Cys
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Cys His Thr Pro Val Thr Asn Glu Glu Thr Glu Ala Arg Glu Ala Lys
20 25 30

Gly Gln Lys Leu Arg Pro Cys His Thr Leu Gly Val His Val Cys Leu
35 40 45

Ser Leu Phe Arg Ser Glu Leu Leu Gly Leu Leu Lys Thr Tyr Asn Cys
50 55 60

Tyr His Glu Gly Lys Ser Phe Gln Leu Arg His Arg Glu Glu Glu Gly
65 70 75 80

Thr Leu Ile Ile Glu Gly Leu Leu Asn Ile Ala Trp Gly Leu Arg Arg
85 90 95

Pro Ile Arg Leu Gln Met Gln Asp Asp Arg Glu Gln Val His Leu Pro
100 105 110

Ser Thr Ser Trp Met Pro Arg Arg Pro Ser Cys Pro Leu Lys Glu Pro
115 120 125

Ser Pro Gln Asn Gly Asn Ile Thr Ala Gln Gly Pro Ser Ile Gln Pro
130 135 140

Val His Lys Ala Glu Ser Ser Thr Asp Ser Ser Gly Pro Leu Glu Glu
145 150 155 160

Ala Glu Glu Ala Pro Gln Leu Met Arg Thr Lys Ser Asp Ala Ser Cys
165 170 175

Met Ser Gln Arg Arg Pro Lys Cys Arg Ala Pro Gly Glu Ala Gln Arg
180 185 190

Ile Arg Arg His Arg Phe Ser Ile Asn Gly His Phe Tyr Asn His Lys
195 200 205

Thr Ser Val Phe Thr Pro Ala Tyr Gly Ser Val Thr Asn Val Arg Val
210 215 220

Asn Ser Thr Met Thr Thr Leu Gln Val Leu Thr Leu Leu Leu Asn Lys
225 230 235 240

Phe Arg Val Glu Asp Gly Pro Ser Glu Phe Ala Leu Tyr Ile Val His
245 250 255

Glu Ser Gly Glu Arg Thr Lys Leu Lys Asp Cys Glu Tyr Pro Leu Ile
260 265 270

Ser Arg Ile Leu His Gly Pro Cys Glu Lys Ile Ala Arg Ile Phe Leu
275 280 285

Met Glu Ala Asp Leu Gly Val Glu Val Pro His Glu Val Ala Gln Tyr
290 295 300

Ile Lys Phe Glu Met Pro Val Leu Asp Ser Phe Val Glu Lys Leu Lys
305 310 315 320

Glu Glu Glu Glu Arg Glu Ile Ile Lys Leu Thr Met Lys Phe Gln Ala
325 330 335

Leu Arg Leu Thr Met Leu Gln Arg Leu Glu Gln Leu Val Glu Ala Lys
340 345 350

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<212> PRT
<213> Homo sapien

<400> 291

Met Ala Val Trp Ser Pro Leu Val Met Pro Gly Arg Arg Glu Gly Cys
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Cys His Thr Pro Val Thr Asn Glu Glu Thr Glu Ala Arg Glu Ala Lys
20 25 30

Gly Gln Lys Leu Arg Pro Cys His Thr Leu Gly Val His Val Cys Leu
35 40 45

Ser Leu Phe Arg Ser Glu Leu Leu Gly Leu Leu Lys Thr Tyr Asn Cys
50 55 60

Tyr His Glu Gly Lys Ser Phe Gln Leu Arg His Arg Glu Glu Glu Gly
65 70 75 80

Thr Leu Ile Ile Glu Gly Leu Leu Asn Ile Ala Trp Gly Leu Arg Arg
85 90 95

Pro Ile Arg Leu Gln Met Gln Asp Asp Arg Glu Gln Val His Leu Pro
100 105 110

Ser Thr Ser Trp Met Pro Arg Arg Pro Ser Cys Pro Leu Lys Glu Pro
115 120 125

Ser Pro Gln Asn Gly Asn Ile Thr Ala Gln Gly Pro Ser Ile Gln Pro
130 135 140

Val His Lys Ala Glu Ser Ser Thr Asp Ser Ser Gly Pro Leu Glu Glu
145 150 155 160

Ala Glu Glu Ala Pro Gln Leu Met Arg Thr Lys Ser Asp Ala Ser Cys
165 170 175

Met Ser Gln Arg Arg Pro Lys Cys Arg Ala Pro Gly Glu Ala Gln Arg
180 185 190

Ile Arg Arg His Arg Phe Ser Ile Asn Gly His Phe Tyr Asn His Lys
195 200 205

Thr Ser Val Phe Thr Pro Ala Tyr Gly Ser Val Thr Asn Val Arg Val
210 215 220

Asn Ser Thr Met Thr Thr Leu Gln Val Leu Thr Leu Leu Leu Asn Lys
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Glu Ser Gly Gly Phe
260

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<400> 292

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Cys His Thr Pro Val Thr Asn Glu Glu Thr Glu Ala Arg Glu Ala Lys
20 25 30

Gly Gln Lys Leu Arg Pro Cys His Thr Leu Gly Val His Val Cys Leu
35 40 45

Ser Leu Phe Arg Ser Glu Leu Leu Gly Leu Leu Lys Thr Tyr Asn Cys
50 55 60

Tyr His Glu Gly Lys Ser Phe Gln Leu Arg His Arg Glu Glu Glu Gly
65 70 75 80

Thr Leu Ile Ile Glu Gly Leu Leu Asn Ile Ala Trp Gly Leu Arg Arg
85 90 95

Pro Ile Arg Leu Gln Met Gln Asp Asp Arg Glu Gln Val His Leu Pro
100 105 110

Ser Thr Ser Trp Met Pro Arg Arg Pro Ser Cys Pro Leu Lys Glu Pro
115 120 125

Ser Pro Gln Asn Gly Asn Ile Thr Ala Gln Gly Pro Ser Ile Gln Pro
130 135 140

Val His Lys Ala Glu Ser Ser Thr Asp Ser Ser Gly Pro Leu Glu Glu
145 150 155 160

Ala Glu Glu Ala Pro Gln Leu Met Arg Thr Lys Ser Asp Ala Ser Cys
165 170 175

Met Ser Gln Arg Arg Pro Lys Cys Arg Ala Pro Gly Glu Ala Gln Arg
180 185 190

Ile Arg Arg His Arg Phe Ser Ile Asn Gly His Phe Tyr Asn His Lys

195 200 205

Thr Ser Val Phe Thr Pro Ala Tyr Gly Ser Val Thr Asn Val Arg Val
210 215 220

Asn Ser Thr Met Thr Thr Leu Gln Val Leu Thr Leu Leu Leu Asn Lys
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Phe Arg Val Glu Asp Gly Pro Ser Glu Phe Ala Leu Tyr Ile Val His
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Glu Ser Gly Glu Asp Arg Gln Asp Leu Pro Asp Gly Ser
260 265

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20 25 30

Asn Thr Glu Val Arg Pro Gly Ile Arg Pro Gln Val Ser His Phe Leu
35 40 45

Cys Arg Asn Gln Ser Leu Leu His Gln Arg Asp Leu Lys Arg Phe Leu
50 55 60

Gln Gly Ala Cys Cys Lys Lys His Gly His Ser Ile Thr Leu Arg Arg
65 70 75 80

Val His Met Ala Leu Arg Gly Cys Cys Pro Leu Asn Ala Gln Gln Gln
85 90 95

Leu Trp Lys Ala Val Leu Ser Pro Ile Thr Thr Val Pro Trp Met Pro
100 105 110

Val Tyr Leu Leu Pro Phe Leu Gly Leu Arg Phe Ser Pro Leu Val Gly
115 120 125

Gly Asp Asp Phe Gln
130

<210> 294
<211> 163
<212> PRT
<213> Homo sapien

<400> 294

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Gly Cys Arg Ile Gly Tyr Gly Arg Ile Trp Ala Glu Thr Trp Ala Ser
20 25 30

Arg Ser Leu Leu Tyr Arg Pro Val His Ser Ser Val Leu Leu Ser Val
35 40 45

Leu Glu Ser Ala Ile Glu Met Thr Thr Leu Cys Ser Asp Ala Leu Cys
50 55 60

Ser Pro Gln Pro Gly Leu Thr Ala Pro His Glu Ala Gln Ala Thr Ala
65 70 75 80

Phe Pro Leu Leu Gly Arg Gly Glu Met Arg Leu Leu Gln Gly Ser Pro
85 90 95

Glu Leu Ala Ile Cys Arg Ser Leu Ala Leu Leu Pro Thr Ser Leu Pro
100 105 110

Cys Leu Ala Ser Val Ser Pro Leu Gly Asp Val Ser Leu Gln Val Pro
115 120 125

Ser Pro Ala Ser Asp Asp Ala Ala Ala Pro Gly Ala Ala Gly Gly Gly
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Gln Val Thr Gly Gln His Leu Pro Leu Pro Lys Ser Pro Ala Val Ala
145 150 155 160

Gly Val His

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20 25 30

Ser Asn Phe Asn Arg Glu Val Ile Gln Ser Asp Ser Leu Trp Leu Val
35 40 45

Glu Phe Tyr Ala Pro Trp Cys Gly His Cys Gln Arg Leu Thr Pro Glu
50 55 60

Trp Lys Lys Ala Ala Thr Ala Leu Lys Asp Val Val Lys Val Gly Ala
65 70 75 80

Val Asp Ala Asp Lys His His Ser Leu Gly Gly Gln Tyr Gly Val Gln
85 90 95

Gly Phe Pro Thr Ile Lys Ile Phe Gly Ser Asn Lys Asn Arg Pro Glu
100 105 110

Asp Tyr Gln Gly Gly Arg Thr Gly Glu Ala Ile Val Asp Ala Ala Leu
115 120 125

Ser Ala Leu Arg Gln Leu Val Lys Asp Arg Leu Gly Gly Arg Ser Gly
130 135 140

Gly Tyr Ser Ser Gly Lys Gln Gly Arg Ser Asp Ser Ser Ser Lys Lys
145 150 155 160

Asp Val Ile Glu Leu Thr Asp Asp Ser Phe Asp Lys Asn Val Leu Asp
165 170 175

Ser Glu Asp Val Trp Met Val Glu Phe Tyr Ala Pro Trp Cys Gly His
180 185 190

Cys Lys Asn Leu Glu Pro Glu Trp Ala Ala Ala Ala Ser Glu Val Lys
195 200 205

Glu Gln Thr Lys Gly Lys Val Lys Leu Ala Ala Val Asp Ala Thr Val
210 215 220

Asn Gln Val Leu Ala Ser Arg Tyr Gly Ile Arg Gly Phe Pro Thr Ile
225 230 235 240

Lys Ile Phe Gln Lys Gly Glu Ser Pro Val Asp Tyr Asp Gly Gly Arg
245 250 255

Thr Arg Ser Asp Ile Val Ser Arg Ala Leu Asp Leu Phe Ser Asp Asn
260 265 270

Ala Pro Pro Pro Glu Leu Leu Glu Ile Ile Asn Glu Asp Ile Ala Lys
275 280 285

Arg Thr Cys Glu Glu His Gln Leu Cys Val Val Ala Val Leu Pro His
290 295 300

Ile Leu Asp Thr Gly Ala Ala Gly Arg Asn Ser Tyr Leu Glu Val Leu
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Leu Lys Leu Ala Asp Lys Tyr Lys Lys Lys Met Trp Gly Trp Leu Trp
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Thr Glu Ala Gly Ala Gln Ser Glu Leu Glu Thr Ala Leu Gly Ile Gly
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Gly Phe Gly Tyr Pro Ala Met Ala Ala Ile Asn Ala Arg Lys Met Lys
355 360 365

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Leu Arg Glu Leu Ser Phe Gly Arg Gly Ser Thr Ala Pro Val Gly Gly
385 390 395 400

Gly Ala Phe Pro Thr Ile Val Glu Arg Glu Pro Trp Asp Gly Arg Asp
405 410 415

Gly Glu Glu Cys Pro Gly Gly Lys Leu Cys Gly Gln Gln Ser Trp Phe
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Thr Leu Leu Ser Leu Cys Ile Ser Ala Pro Gly Val Lys Ser Phe Pro
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Ser Asp Leu Ser Pro Gly Ala Pro Val Gly Leu Leu Arg Gly Ser Ser
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RAW SEQUENCE LISTING
PATENT APPLICATION: **PCT/US03/38855**

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3 <110> APPLICANT: diaDexus, Inc.
4 Macina, Roberto
5 Turner, Leah
6 Sun, Yongming
7 Liu, Shu-Hui
8 Chen, Huei-Mei
10 <120> TITLE OF INVENTION: Compositions, Splice Variants and Methods Relat:
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11 Genes and Proteins
13 <130> FILE REFERENCE: DEX-0455
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C--> 15 <141> CURRENT FILING DATE: 2003-12-08
15 <150> PRIOR APPLICATION NUMBER: US 60/431,321
16 <151> PRIOR FILING DATE: 2002-12-06
18 <150> PRIOR APPLICATION NUMBER: US 60/431,301
19 <151> PRIOR FILING DATE: 2002-12-06
21 <150> PRIOR APPLICATION NUMBER: US 60/484,584
22 <151> PRIOR FILING DATE: 2003-06-30
24 <150> PRIOR APPLICATION NUMBER: US 60/518,607
25 <151> PRIOR FILING DATE: 2003-11-07
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32 <211> LENGTH: 4798
33 <212> TYPE: DNA
34 <213> ORGANISM: Homo sapien
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41 gcaagactcg tggctgtgac ccatgggcct ctgaggaggc gttgtaagtc cgcccagctc 180
43 cccacttgct gtgctctcac tcaatgcgaa gggaaccaag gtaccagggc caagtgggtc 240
45 cagacatcca cacggattct gaaagggcag gtcaagcaga ctttgtccag ccatcagcca 300
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RAW SEQUENCE LISTING
PATENT APPLICATION: **PCT/US03/38855**

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Output Set: **N:\CRF4\12292003\PU38855.raw**

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PATENT APPLICATION: **PCT/US03/38855**

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RAW SEQUENCE LISTING
PATENT APPLICATION: **PCT/US03/38855**

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Output Set: **N:\CRF4\12292003\PU38855.raw**

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RAW SEQUENCE LISTING ERROR SUMMARY
PATENT APPLICATION: PCT/US03/38855

Input Set : N:\FANTU\0338855.txt
Output Set: N:\CRF4\12292003\PU38855.raw

Please Note:
Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220> to <223> fields of each sequence which presents at least one n or Xaa.

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Seq#:233; Xaa Pos. 81,83,97,115
Seq#:234; Xaa Pos. 9,10,16,17,37,40,45,47,87
Seq#:237; Xaa Pos. 70,84,92
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VERIFICATION SUMMARY
PATENT APPLICATION: **PCT/US03/38855**

Input Set : **N:\FANTU\0338855.txt**
Output Set: **N:\CRF4\12292003\PU38855.raw**

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(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
24 June 2004 (24.06.2004)

PCT

(10) International Publication Number
WO 2004/053079 A3

(51) International Patent Classification[7]: C12N 15/12, 15/11, 15/00, C12Q 1/68, C12P 21/02, A61K 31/7088, 31/711

(21) International Application Number: PCT/US2003/038855

(22) International Filing Date: 8 December 2003 (08.12.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/431,321	6 December 2002 (06.12.2002)	US
60/431,301	6 December 2002 (06.12.2002)	US
60/484,584	30 June 2003 (30.06.2003)	US
60/518,607	7 November 2003 (07.11.2003)	US

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(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report: 7 April 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2004/053079 A3

(54) Title: COMPOSITIONS, SPLICE VARIANTS AND METHODS RELATING TO OVARIAN SPECIFIC GENES AND PROTEINS

(57) Abstract: The present invention relates to newly identified nucleic acid molecules and polypeptides present in normal and neoplastic ovarian cells, including fragments, variants and derivatives of the nucleic acids and polypeptides. The present invention also relates to antibodies to the polypeptides of the invention, as well as agonists and antagonists of the polypeptides of the invention. The invention also relates to compositions containing the nucleic acid molecules, polypeptides, antibodies, agonists and antagonists of the invention and methods for the use of these compositions. These uses include identifying, diagnosing, monitoring, staging, imaging and treating ovarian cancer and non-cancerous disease states in ovarian, identifying ovarian tissue, monitoring and identifying and/or designing agonists and antagonists of polypeptides of the invention. The uses also include gene therapy, production of transgenic animals and cells, and production of engineered ovarian tissue for treatment and research.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/38855

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : C12N 15/12, 15/11, 15/00; C12Q 1/68; C12P 21/02; A61K 31/7088, 31/711
US CL : 536/23.1, 23.5; 435/6, 320.1, 69.1; 514/44
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 536/23.1, 23.5; 435/6, 320.1, 69.1; 514/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Compugen, SEQ ID NOs: 1 and 129

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	NETO, E.D. et al, Shotgun sequencing of the human transcriptome with ORF expressed sequence Tags. Proceedings of the National Academy of Science, USA. 28 March 2000, Vol. 97, No. 7, pages 3491-3496, see especially the alignment attached to the reference (compare SEQ ID NO: 1, nucleotides 221-522 to BX281918, nucleotides 1-302).	1-6, 8, and 9 ----------- 10

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search 11 January 2005 (11.01.2005)	Date of mailing of the international search report 31 JAN 2005
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer James Martinell Telephone No. 571-272-1600

Form PCT/ISA/210 (second sheet) (July 1998)

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-10 and 15-18 as they pertain to nucleic acids encoding SEQ ID NO: 129

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-10 and 15-18, drawn to nucleic acids, nucleic acid molecular hybridization assays, vectors, host cells, methods for producing polypeptides, kits, vaccines, and methods of treatment using nucleic acids.

Group II, claim(s) 11, 12, and 16-18, drawn to polypeptides, kits, vaccines, and methods of treatment using polypeptides.

Group III, claim(s) 13-15, drawn to antibodies and protein binding assays.

The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The nucleic acids, vectors, host cells, nucleic acid containing kits, nucleic acid vaccines, and methods of treatment using nucleic acids of Group I all have the special technical features of the properties of SEQ ID NOs: 129-295 or nucleic acid sequences that encode SEQ ID NOs: 1-128, which are not shared by either of Groups II or III. Group II is directed to polypeptide, polypeptide vaccines, and methods of treatment using polypeptides that all have the special technical features of SEQ ID NOs: 1-128 or sequences that are encoded by SEQ ID NOs: 129-295, which are not shared by Groups I or III. Since each of the three Groups mentions or requires the use of 295 separate and unrelated nucleic acids and/or polypeptides, the total number of inventions is 3 x 295 = 885.

Each of the Groups mentions or requires the use of a large number (295) of separate and unrelated nucleic acids and/or polypeptides. No matter which additional Group(s) applicant elects, applicant is further required to select for search one SEQ ID NO within the Group(s) for search. In any event, the first mentioned SEQ ID NO in Group I will be searched. Any additional SEQ ID NO to be searched requires one additional search fee per SEQ ID NO. In the absence of payment of additional search fee(s) only the first mentioned SEQ ID NO in Group I will be searched. Should applicant pay fee(s) for additional Groups to be searched, the first mentioned SEQ ID NO within the selected Group will be searched unless applicant directs otherwise.